



# MEDICAL CLASSICS

VOL. I

September, 1936

NO. 1



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## A Preface Concerning Aims and Policy

**M**ANY doctors are not interested in medical history, that is, in medical history as it has been served to them up to the present time. This is a sad and unnatural state of affairs. Our debt to the past was thus expressed by Claude Bernard: "We stand upon the intellectual shoulders of those medical giants of bygone days and, because of the help they afford us, we are able to see a little more clearly than they were able to do."

MEDICAL CLASSICS aims to awaken the interest of all medical workers in the historical side of their profession. The work will be useful, not merely ornamental.

As an example, the subject chosen for the first number is Sir James Paget and his papers on osteitis deformans or Paget's disease of the bones and his paper on Paget's disease of the nipple. These and all papers published will be as the author wrote them. They will not be abstracted according to the whim of the editor or the convenience of the publisher.

We believe that every doctor who has a patient with osteitis deformans or one in whom osteitis deformans is a possibility will be a better doctor if he knows intimately the writings of Paget on this subject. Today we know no more about the disease than Paget did. In the same way, the problem of Paget's disease of the nipple is still unsolved and is the subject of frequent controversy. How important it is to know just what Paget described in his original paper!



How many doctors know the location of McBurney's point? About forty percent of medical texts do not locate this point where McBurney described it. Obviously this leads to confusion, inexact terms and differences of medical opinion. We will republish McBurney's original papers in which he describes the point and also the incision which go by his name.

The following list of subjects will appear in early issues of MEDICAL CLASSICS: Addison's disease, Argyll Robertson pupil, Banti's disease, Bassini operation, Bell's law, nerve and palsy, Billroth's operation, Brodie's abscess, pile and tumor, Bryant's triangle, Buck's extension, Colles's fracture, Corrigan's disease and pulse, Dercum's disease, Dupuytren's contracture, Fowler's position, Graves's disease, Halsted's operations for cancer of breast and hernia, Hodgkin's disease, Mikulicz's disease and resection, Morton's metatarsalgia, Murphy button, drip and treatment, Parkinson's disease, Pott's disease of spine and fracture, Raynaud's disease, Stokes-Adams's disease, Thomas splints and Trendelenburg operation and position.

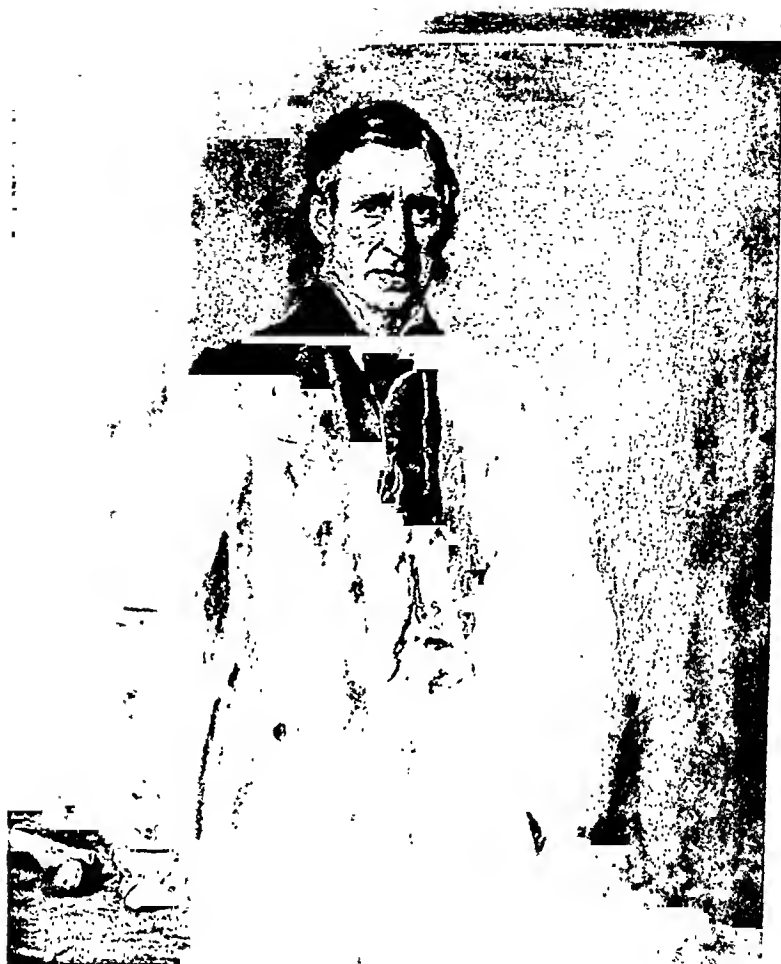
In addition to these, papers of outstanding progress in medicine will be published from time to time. Here we include Oliver Wendell Holmes' *The Contagiousness of Puerperal Fever*, Robert Koch's *The Etiology of Tuberculosis* and Koch's postulates, Lord Lister's *On a New Method of Treating Compound Fracture* and Ephraim McDowell's *Three Cases of Extirpation of Diseased Ovaries*.

Suggestions as to papers to be included or policy to be pursued will be appreciated. We are grateful for the many suggestions that have already been received.

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*Medical Classics* is dedicated to Dr. JOSEPH LEWI DONHAUSER whose forbearance and stimulation have made this work possible.





*Ever yours*  
*James Paget.*

SIR JAMES PAGET

From a painting by Sir John Millais, 1872, with a signature written in 1891. Reproduced from *Memoirs and Letters of Sir James Paget*, edited by Stephen Paget, third edition, London, Longmans, Green & Co., 1903.



# Sir James Paget

## BIOGRAPHY

- 1814 Born January 11, in Great Yarmouth, England, eighth of seventeen children. Father was a brewer and ship-owner, and mayor in 1817. Educated at private school in Yarmouth.
- 1830 Age 16. Apprenticed to Charles Costerton, a graduate of St. Bartholomew's Hospital, in practice in Yarmouth.
- 1834 Age 20. Went to London to enter medical school of St. Bartholomew's Hospital. While dissecting during freshman year discovered the trichina spiralis.
- 1836 Age 22. May 13, became member of Royal College of Surgeons of England. Visited in Paris and then settled in London where he supported himself by writing and teaching.
- 1837 Age 23. Appointed curator of St. Bartholomew's Hospital Museum. Became sub-editor of Medical Gazette.
- 1839 Age 25. Chosen demonstrator of morbid anatomy.
- 1841 Age 27. Appointed surgeon to Finsbury dispensary.
- 1843 Age 29. Promoted to lecturer on general anatomy and physiology. Elected warden of college for students at St. Bartholomew's.
- 1844 Age 30. Married Lydia North, by whom he had four sons and two daughters.
- 1847 Age 33. Chosen assistant surgeon to St. Bartholomew's.
- 1851 Age 37. Elected F.R.S.
- 1858 Age 44. Appointed surgeon-extraordinary to the Queen.
- 1859 Age 45. Lecturer on physiology.
- 1860 Age 46. Appointed member of senate of University of London.

- 1861 Age 47. Promoted to full surgeon.
- 1865 Age 51. Held lectureship on surgery.
- 1869 Age 55. President of the Clinical Society of London.
- 1871 Age 57. Resigned as surgeon and appointed a consulting surgeon to St. Bartholomew's Hospital. Created baronet.
- 1874 Age 60. Described eczema of nipple with subsequent mammary cancer (Paget's disease of the nipple).
- 1875 Age 61. President of the Royal College of Surgeons. President of Royal Medical and Chirurgical Society.
- 1876 Age 62. Appointed sergeant-surgeon to Queen Victoria on death of Sir William Fergusson.  
Described osteitis deformans (Paget's disease of the bones).
- 1881 Age 67. President of International Congress of Medicine held in London.
- 1883 Age 69. Vice-chancellor of University of London until 1895.
- 1887 Age 73. President of Pathological Society of London.
- 1899 Age 85. December 30, died at his house, 5 Park Square West, Regent's Park. Buried in Finchley Cemetery after funeral service in Westminster Abbey.  
Held also honorary degrees of D.C.L. (Oxford), LL.D. (Cambridge), F.R.C.S. (Edinburgh and Ireland), M.D. (Dublin, Bonn, Wurzburg).

## EPONYMS

1. ABSCESS: An abscess recurring about the residue of a former abscess; a residual abscess. *On residual abscesses.* St. Barth. Hosp. Rep., 5: 73-79, 1869.
2. DISEASE OF THE BONES: Osteitis deformans. *On a form of chronic inflammation of bones—osteitis deformans.* Trans. Med. Chir. Soc., 60: 37-64, 1877. *Additional cases of osteitis deformans, notes on seven cases.* Ibid., 65: 225-236, 1882. *Remarks on osteitis deformans.* Illust. Med. News, 2: 181-182, 1889.

3. DISEASE OF THE NIPPLE: An inflammatory, eczematoid affection of the areola and nipple, followed by cancer of the breast. *On diseases of the mammary areola preceding cancer of the mammary gland.* St. Barth. Hosp. Rep., 10: 87-89, 1874.
4. MIXTURE: Haustus hydrargyri perchloridi cum potassii iodido. Its formula is: solution of perchloride of mercury, one fluid drachm; iodide of potassium, five grains; compound tincture of cardamonis, twenty minims; distilled water to one fluid ounce. St. Barth. Hosp. Pharmacopeia, edition of 1882.
5. TUMOR: Recurrent fibroid, desmoid tumor or cellular fibroma, usually occurring in the abdominal wall (rectus) of young women. *Recurring fibroid and fibro-nucleated tumors.* *Lectures on Surgical Pathology.* London, Longman, 2: 155, 1853.

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## PAGET'S DISEASE OF BONE

At the age of 57, Sir James Paget resigned as active surgeon to St. Bartholomew's Hospital and became consulting surgeon. The additional time obtained by thus relinquishing a busy service was employed in medical writing and lecturing. At the age of 60, Paget published his paper *On disease of the mammary areola preceding cancer of the mammary gland*, and, at the age of 62, wrote his famous article *On a form of chronic inflammation of bones—osteitis deformans*, following it, at the age of 68, with seven additional cases of this condition. See these complete papers in the following pages.

After publishing the original paper, Paget discovered that the term *osteitis deformans* had been used a few years previously by Czerny, by Schmidt and by Volkmann for other conditions. This was acknowledged in the second report. But Paget's article is so complete, his clinical picture so clear-cut, and his histopathologic descriptions so exact that the term is now confined to the disease he described and his name is inseparably linked with the condition.

Although all the features of Paget's disease of bone have long been recognized and have received careful study, the etiology is still unknown. Paget himself, largely by negative inference, thought the condition an inflammatory one. More recent writers have put forth other theories; Richard in 1887 compared the condition to arthritis deformans; Gilles de la Tourette and Marinesco in 1895 found lesions in the central nervous system; LeWald in 1917 believed the disease the antithesis of acromegaly and due to some pituitary gland disturbance. Interesting reviews of the problem have been published by A. W. Elting (Johns Hopkins Hosp. Bull., 12: 343-349, 1901), by P. Lewin (Jour. Bone & Joint Surg., 4: 45-67, 1922; 7: 279-285, 1925), and by E. C. Cutler (Boston Med. & Surg. Jour., 174: 187-192, 1916). More recently, R. J. M. Love (Clin. Jour., 60: 178, 1931), F. G. Murphy (Jour. Bone & Joint Surg., 16: 981-985, 1934), and C. A. Traver (N. Y. State Jour. Med., 36: 242-246, 1936) have added to our knowledge of the association of Paget's disease of bone with fractures.

ON A FORM  
OF  
CHRONIC INFLAMMATION OF BONES  
(OSTEITIS DEFORMANS).

BY  
SIR JAMES PAGET, BART., D.C.L., LL.D., F.R.S.,  
CONSULTING SURGEON TO ST. BARTHOLOMEW'S HOSPITAL, ETC.

Received November 1st—Read November 14th, 1876.

I HOPE it will be agreeable to the Society if I make known some of the results of a study of a rare disease of bones.

The patient on whom I was able to study it was a gentleman of good family, whose parents and grandparents lived to old age with apparently sound health, and among whose relatives no disease was known to have prevailed. Especially, gout and rheumatism, I was told, were not known among them; but one of his sisters died with chronic cancer of the breast.

Till 1854, when he was forty-six years old, the patient had no sign of disease, either general or local. He was a tall, thin, well-formed man, father of healthy children, very active in both mind and body. He lived very temperately, could digest, as he said, anything, and slept always soundly.

At forty-six, from no assigned cause, unless it were that he lived in a rather cold and damp place in the North of England, he began to be subject to aching pains



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At forty-six, from no assigned cause, unless it were that he lived in a rather cold and damp place in the North of England, he began to be subject to aching pains in his thighs and legs. They were felt chiefly after active exercise, but were never severe;

yet the limbs became less agile or, as he called them, "less serviceable," and after about a year he noticed that his left shin was misshapen. His general health was, however, quite unaffected.

I first saw this gentleman in 1856, when these things had been observed for about two years. Except that he was very grey and looked rather old for his age, he might have been considered as in perfect health. He walked with full strength and power, but somewhat stiffly. His left tibia, especially in its lower half, was broad, and felt nodular and uneven, as if not only itself but its periosteum and the integuments over it were thickened. In a much less degree similar changes could be felt in the lower half of the left femur. This limb was occasionally but never severely painful, and there was no tenderness on pressure. Every function appeared well discharged, except that the urine showed rather frequent deposits of lithates. Regarding the case as one of chronic periostitis, I advised iodide of potassium and *Liquor Potassæ*; but they did no good.

Three years later I saw the patient with Mr. Stanley. He was in the same good general health, but the left tibia had become larger, and had a well-marked anterior curve, as if lengthened while its ends were held in place by their attachments to the unchanged fibula. The left femur also was now distinctly enlarged, and felt tuberos at the junction of its upper and middle thirds, and was arched forwards and outwards, so that he could not bring the left knee into contact with the right. There was also some appearance of widening of the left side of the pelvis, the nates on this side being flattened and lowered, and the great trochanter projecting nearly half an inch further from the middle line. The left limb was about a quarter of an inch shorter than the right. The patient believed that the right side of his skull was enlarged, for his hats had become too tight; but the change was not clearly visible.

Notwithstanding these progressive changes, the patient suffered very little; he had lived actively, walking, riding, and engaging in all the usual pursuits of a country gentleman, and, except that his limb was clumsy, he might have been indifferent to it. He had taken various medicines, but none had done any good, and iodine, in whatever form, had always done harm.

In the next seventeen years of his life I rarely saw him, but the story of his disease, of which I often heard, may be briefly told and with few dates, for its progress was nearly uniform and very slow. The left femur and tibia became larger, heavier, and somewhat more curved. Very slowly those of the right limb followed the same course, till they gained very nearly the same size and shape. The limbs thus became nearly symmetrical in their deformity, the curving of the left being only a little more outward than that of the right. At the same time, or later, the knees became gradually bent, and, as if by rigidity of their fibrous tissues, lost much of their natural range and movement.

The skull became gradually larger, so that nearly every year, for many years, his hat, and the helmet that he wore as a member of a Yeomanry Corps needed to be enlarged. In 1844 he wore a shako measuring twenty-two and a half inches inside; in 1876 his hat measured twenty-seven and a quarter inches inside (Pl. I, fig. 4). In its enlargement, however, the head retained its natural shape and, to the last, looked intellectual, though with some exaggeration.

The changes of shape and size in both the limbs and the head were arrested, or increased only imperceptibly, in the last three or four years of life.

The spine very slowly became curved and almost rigid. The whole of the cervical vertebræ and the upper dorsal formed a strong posterior, not angular, curve; and an anterior curve, of similar shape, was formed by the lower dorsal and lumbar vertebræ. The length of the spine thus seemed lessened, and from a height of six feet one inch he sank to about five feet nine inches. At the same time the chest became contracted, narrow, flattened laterally, deep from before backwards, and the movements of the ribs and of the spine were lessened. There was no complete rigidity, as if by union of bones, but all the movements were very restrained, as if by shortening and rigidity of the fibrous connections of the vertebræ and ribs.

The shape and habitual posture of the patient were thus made strange and peculiar. His head was advanced and lowered, so that the neck was very short, and the chin, when he held his head

at ease, was more than an inch lower than the top of the sternum.

The short narrow chest suddenly widened into a much shorter and broad abdomen, and the pelvis was wide and low. The arms appeared unnaturally long, and, though the shoulders were very high, the hands hung low down by the thighs and in front of them. Altogether, the attitude in standing looked simian, strangely in contrast with the large head and handsome features.\*

All the changes of shape and attitude are well shown in sketches from photographs taken six months before death (see Pl. I, figs. 1 to 3). Only the lowering of the necks of the femora is not shown. In measurement after death the axes of the shaft and neck of the right femur formed an angle of only  $100^\circ$  instead of  $120^\circ$  or  $125^\circ$ , and this change of shape added to the appearance of increased width of the pelvis.

But with all these changes in shape and mobility of the head, spine, and lower limbs, the upper limbs remained perfect, and there was no disturbance of the general health.

In 1870, when the disease had existed sixteen years, the left knee-joint was, for a time, actively inflamed and its cavity was distended with fluid. But the inflammation soon subsided, only leaving the joint stiffer and more bent.

About this time some signs of insufficiency of the mitral valve were observed, but the patient now lived so quietly, and moved with so little speed, that this defect gave him no considerable distress.

In December, 1872, sight was partially destroyed by retinal hæmorrhage, first in one eye, then in the other,† and at nearly the same time he began to be somewhat deaf. In the summer of 1874 he had frequent cramps in the legs, and neuralgic pains, which were described as “jumping over all the upper part of the body except the head,” but change of air seemed to cure them.

\* An attitude somewhat similar is given by a rare form of what I suppose to be general chronic rheumatic arthritis of the spine involving its articulations with the ribs. The spine droops and is stiff, the chest is narrow, the ribs scarcely move, the abdomen is low and broad, but there is no deformity of head or limbs.

† Mr. Brudenell Carter saw him in January, 1873, and observed “the right retina sprinkled with small dots of arterial hæmorrhage, chiefly in parts remote from the centre;” and “there was no other change.” The left retina was at this time healthy, but in February Dr. Clifford Allbutt found “several little plugs” in its vessels.

In January, 1876, he began to complain of pain in his left forearm and elbow which, at first, was thought to be neuralgic. But it grew worse, and swelling appeared about the upper third of the radius and increased rapidly, so that, when I saw him in the middle of February, it seemed certain that a firm medullary or osteoid cancerous growth was forming round the radius.

Still the general health was good. Auscultation could detect mitral disease, but the appetite and digestion were unimpaired, the urine was healthy, the mind as clear, patient, and calm as ever. As letters about him at this time said "his general health has been excellent;" "he is free from pain except in the left arm; he sleeps well, enjoys himself, and does not know what a headache is."

After this time, however, together with rapid increase of the growth upon the radius, there were gradual failure of strength and emaciation, and on the 24th of March, after two days of distress with pleural effusion on the right side, he died.

The body was examined five days after death, and showed no marked signs of decomposition. As it lay on a flat board its posture was remarkable, for the head was upraised to the level of the sternum, being supported by the rigid and arched spine, and the lower limbs, with the knees bent and stiff, rested on the heels and nates.

The pericranium, dura mater and all the substance of the brain appeared healthy.

The right pleural cavity contained at least a pint of pale serous fluid, with flakes and strings of inflammatory exudation. The lung was compressed, and in its pleural covering were numerous small nodular masses of pale cancerous substance. The proper pulmonary structure appeared healthy, and so did the left lung and its pleura, except that in the pleura and anterior mediastinum there were many small masses of cancer.

The heart was enlarged but thin-walled. The tricuspid and pulmonary valves and artery were healthy; the mitral valve was opaque, contracted, stiffened with atheromatous and calcareous deposits.

The aortic valves were slightly opaque but pliant, and both in



them and in the first part of the aorta were numerous small patches of atheroma.

The liver and digestive canal and kidneys, examined externally, appeared healthy.

The right femur, the left tibia, the patellæ, and the upper part of the skull, were taken for separate examination, and will be separately described.

In the other bones of the skeleton, except the left radius, no signs of disease appeared externally, but I regret that they were not all more carefully examined, for I think that, at least in the clavicles and pelvis, some changes like those in the long bones of the lower limbs would have been found.

The upper third of the left radius was involved in a large ovoid mass of pale grey and white soft cancerous substance, similar to that of the nodules in the pleuræ and mediastinum, but with growths of bone extending into it. The rest of the radius and the ulna appeared quite healthy.

Some nodules of similar cancerous substance were imbedded in the bones of the vault of the skull.

Microscopic sketches of these structures by Mr. Butlin are appended (Plate II, figs. 1-3).

The curvatures of the spine and its rigidity appeared due to shortening and hardening of its fibrous structures. The vertebæ appeared healthy; there was no appearance of overgrowth or ankylosis among them.

In no part, whether near or far from the diseased bones, was there an indication of any change of structure in skin, muscle, tendon, or fascia; but in the right hip-joint and in the left knee-joint there was some thinning and wasting of articular cartilage, such as one sees in chronic rheumatic arthritis. The other hip- and knee-joints and both ankle-joints were healthy.

In the arteries of the lower limbs there was extensive atheromatous and calcareous degeneration.

The enlargement of the skull may be estimated by comparison of the following measurements:

	<i>Diseased skull</i>	<i>Average skull</i>
Circumference at the level of the middle of the temporal fossa.	26½ in.	21 in.
From occipital spine to base of nasal bones. . . . .	15 in.	13¼ in.
From mastoid to mastoid process. . . . .	18½ in.	15¼ in.

All the sutures, at least all those of the vertex, were obliterated. The outer surface of the upper part of the skull was lowly bossed by the predominant thickening of the hinder part of the parietal bones. The thickness was in every part increased to the extent shown in these following measurements.

In a median vertical section the thickness of the frontal bone was.	11-13 lines.
In a median vertical section the thickness of the parietal bone was..	14-16 lines.
In a median vertical section the thickness of the occipital bone was..	8-12 lines.
In a horizontal section, through the middle of the temporal fossa:	
The thickness of the frontal bone was. . . . .	8-9 lines.
The thickness of the temporal bone was. . . . .	6-9 lines.
The thickness at their junction was. . . . .	2 lines.
The thickness of the occipital bone was. . . . .	10-12 lines.

Comparing these measurements with those of average healthy skulls, it may be said that the bones of the vault of this skull were in every part increased to about four times the normal thickness.

The whole outer surface of the skull-cap was finely porous; in the least changed parts, such as the squamous bone, perforated with innumerable apertures for blood-vessels; in the most changed, finely reticulate, as with delicate cancellous and medullary texture.

The inner surface was comparatively smooth and appeared little changed, except by the enlargement of all channels and apertures for blood-vessels, and especially by the deepening of all the grooves for the middle meningeal artery and its branches.

On the cut surface, in the median vertical section, that which might be regarded as the altered internal table of the skull was a layer, having a very unequal thickness varying from two to six lines, consisting of hard white bone, close-textured, in some parts porous or finely reticulate, in more looking compact and dense like limestone or white brick (Pl. V).

The rest of the thickness of this part of the skull, representing probably the altered diploë and outer table, was made up of

bone in various degrees porous, cancellous, or cavernous, with spaces filled with soft reddish substance, a kind of medulla. Its surface was covered with a very thin layer, a mere coating of more finely porous bone.

In the horizontal section, at the level of the upper part of the squamous bone, the same altered characters were observable, but a larger proportion of the substance of the skull was finely porous or reticulate.

By the cavities in the skull-cap in which cancerous growths were lodged the structure of the bone was neither more nor less altered than in other parts.

A portion of sphenoid bone showed changes of structure very similar to those already described, but with a much more uniform and regular finely porous condition.

The bones of the face were not uncovered, but they showed, neither to sight nor touch, any appearance of disease; not a feature was unnatural.

The conditions of all the long bones were so similar that one description may serve for the altered structure of both femora and tibiæ.\*

The periosteum was not visibly changed, not thicker or more than usually adherent.

The outer surface of the walls of the bones was irregularly and finely nodular, as with external deposits or outgrowths of bone, deeply grooved with channels for the larger periosteal blood-vessels, finely but visibly perforated in every part for transmission of the enlarged small vessels. Everything seemed to indicate a greatly increased quantity of blood in the vessels of the bone.†

The medullary structures appeared to the naked eye as little changed as the periosteum. The medullary spaces were filled with soft, yellow, ruddy, and bright crimson medulla, of apparently healthy consistence. The medullary laminæ and cancelli had a normal aspect and arrangement, and in the shafts of the long bones the medullary spaces were not encroached upon.

\* Their changes are shown in Pl. IV. The specimens are in the Museums of the Royal College of Surgeons and of St. Bartholomew's Hospital.

† But see the account of the microscopic examination.

The compact substance of the bones was, in every part, increased in thickness. Taking, for example, the femur, the thicknesses of its walls and those of a healthy femur of about the same length and age are compared in the following tables.

	Healthy Lines	Diseased Lines
Thickest parts of the wall. ....	3-6	6-10
Articular covering of head, about. ....	$\frac{1}{4}$	3-10
Wall of neck, about. ....	$\frac{1}{4}$ -3	4-6
Wall of the trochanter major, about. ....	$\frac{1}{4}$ - $\frac{1}{2}$	3-5
Articular covering of the condyles, about. ....	$\frac{1}{4}$ - $\frac{1}{2}$	3-5
Lateral walls of the condyles. ....	$\frac{1}{6}$ - $\frac{1}{4}$	2 and more.

Changes in similar proportions were found in the walls of the tibia. In the patellæ the walls were from three to five lines thick.

The thickening of the walls of the shafts of the bones appeared due chiefly to outward expansion and some superficial outgrowth. In some places there were faint appearances of separation of parts of the outer layers of the walls, and of these becoming thick and porous, while the corresponding parts of the inner layers were less changed; but in the greater part of the walls the whole construction of the bone was altered into a hard, porous or finely reticulate substance, like very fine coral. In some places, especially in the walls of the femur, there were small, ill-defined patches of pale, dense, and hard bone looking as solid as brick.

In the compact covering of the articular ends of the long bones, and in those of the neck and great trochanter of the femur, and in the patellæ the increase of thickness was due to encroachment on the cancellous texture, as if by filling of its spaces with compact porous, new-formed bone.

Mr. Butlin was so good as to make careful microscopic examination of the diseased bones, and to give me the following report on them, together with the annexed drawings of their minute structure.

"Microscopical examination was made of sections cut from the skull and from the tibia, some of them from the recent bones, but the majority of them from portions of bone deprived of earthy salts and rendered sufficiently soft to be cut with a razor. The appearances observed were essentially the same in both bones,

but most of the drawings and description were taken from the tibia, the sections of which were much clearer than those of the skull.

"The examination was conducted from a twofold point of view: first, to discover the changes which the bone had undergone; second, to discover, if possible, the nature of the process which had led to such changes.

"With a low power the number of Haversian systems and canals in any given section was seen to be much diminished (Plate II, fig. 8; Plate III, fig. 9). The space between the Haversian canals was occupied by ordinary bone-substance, containing numerous lacunæ and canaliculi. The Haversian canals were enormously widened, many of them were confluent, and thus the appearance of a number of communicating medullary spaces was obtained, an appearance which was rendered still more striking by the presence in the canals of a large quantity of ill-developed tissue in addition to the blood-vessels (Plate II, figs. 4-6). With a high power the contents of the Haversian canals were seen to consist generally of a homogeneous or granular basis, containing cells of round or oval form about the size and having much the appearance of leucocytes. Larger nucleated cells were also present, and fibres or fibro-cells, sometimes in considerable quantity. Myeloid cells were occasionally observed, but they were not plentiful; fat also existed in many of the larger spaces, especially in the skull. The vessels were usually small compared with the channels in which they ran; indeed, they did not seem to be much larger than those of normal bone (Plate II, fig. 6). The walls of some of the canals were lined by a single layer of osteoblasts, a condition precisely similar to that observed in the normal ossification of bone in membrane. The presence of new bone was most evident in the periosteum of the tibia, external to the ordinary compact layer of the shaft (Plate II, fig. 7). This external layer was, of course, but thin, and was much softer and less developed than the cortex of the bone from which it sprung; it evidently was not nearly sufficient to account for the great increase in the diameter of the tibia. From the diminution in size of the medullary canal it was thought that a similar recent

formation of bone would be found on its outskirts, but this expectation was not justified by observation.

"With a medium power the number of (Plate III, fig. 12) lamellæ surrounding the Haversian canals was easily seen to be not larger than in normal bone, whilst the arrangement of the intervening space was most complex and totally different from that of healthy bone. The lacunæ and canaliculi throughout the sections did not strikingly differ from those of ordinary bone."

I am indebted to Dr. Russell for the following chemical analysis of portions of the diseased skull and tibia, and of a healthy tibia in comparison with them.

	Skull	Tibia	Normal tibia
Inorganic constituents (Ash).....	60.59	61.22	63.62
Organic constituents.....	39.41	38.78	36.38
Phosphoric acid ( $P_2O_5$ ).....	22.76	25.45	25.50
Carbonic acid ( $CO_2$ ).....	3.59	3.95	3.59
Fat.....	6.83	3.45	—
Moisture in the sample (dried at $115^{\circ}C$ ).....	15.49	11.83	9.73
The $CO_2$ calculated as calcium carbonate ( $CaCO_3$ ).....	8.17	8.99	8.16
The $P_2O_5$ calculated as calcium phosphate ( $Ca_3P_2O_4$ )..	49.70	55.56	55.66
Specific gravity.....	1.895	1.889	1.886*

\* Specific gravity of normal skull 1.990.

Cases of the disease which I have described are so rare that I believe no one has seen a sufficient number of them to enable him to distinguish this disease, either clinically or anatomically, from some which seem like it. Specimens illustrating it are commonly included under a general name of hyperostosis, osteoporosis, senile rachitis, or the like. But I hope that, if I add to the description I have just given some notes of similar cases which I have seen or found on record, the disease may be so distinguished as to deserve in pathology a separate place and name.

CASE 2.—Some ten years ago I saw a gentleman, between fifty and sixty, very active, tall, thin, and muscular, a master of hounds. For many years before his death he had curvature of the thighs and legs, exactly like that already described, and stooping of the spine. The changes of the limbs were attended with

severe pains, which he used to relieve with hard rubbing, but the general health was unimpaired. In the last years of his life the upper part of his right humerus became very large, and as he was riding and suddenly raised his arm the bone broke near the shoulder. The evidence of large tumour now became clear, and I amputated the arm at the shoulder-joint. The tumour was well marked and very vascular medullary cancer investing and infiltrating the upper part of the humerus. The rest of the humerus was healthy, and the fracture, which was just below its neck, was evidently due to muscular force acting on its structures spoiled by the cancerous growth. He died a few days after the operation, but was not examined after death. The similarity of his case with that which I have described is, I think, certain.

CASE 3.—I saw, with the late Dr. Brinton, a gentleman between forty and fifty who may be still living. He was a sturdy and quite healthy man; his tibiæ were curved and enlarged exactly like those in the first case and he had similar pains, but there was more thickening of periosteum and an appearance of more external formation of bone. He was treated with iodide of potassium and many other things as for periostitis, but without avail.

CASE 4.—A case is recorded by Dr. Wilks in the 'Transactions' of the Pathological Society,\* and through the kindness of Sir William Gull, whom the patient occasionally consulted, I am enabled to add some facts to those in Dr. Wilks's report, and to show photographic portraits.

A summary of Dr. Wilks's report is that the patient was sixty when he died. Signs of the disease, beginning with pains like those of rheumatism in the legs, were first observed fourteen years before his death. It was soon found that the tibiæ were enlarged, and in subsequent years the cranium and nearly all the bones of the skeleton underwent similar changes. About a year before death the general health began to suffer from the thorax having become implicated in the disease. Gradually the chest became more contracted and at last quite fixed; the breathing became

\* Vol. xx, p. 273, 1869.

more difficult until at last the respiratory apparatus altogether stopped.

Sir William Gull's notes tell that the patient consulted him when fifty-six years old, and said that he first noticed enlargement in the left tibia when he was forty-five years old; that he had seven brothers well and strong, and was eldest in the family. He complained chiefly of weakness, inability to make exertion, feeling of nervousness with occasional vertigo, shortness of breath, stiffness in neck, hoarseness and feebleness of voice. His general health was good; he was not much troubled with pain anywhere; but had occasional strange sensations about the head, and much cough. His height, when a young man, was five feet three and a half inches, now four feet eleven and a half inches. The urine was normal and of normal colour. The cranium was enlarged and thickened; the clavicles much thickened, as also the long bones; the phalanges and facial bones and perhaps the lower jaw were not altered. The ribs were thick and immovable, as was also the sternum. There was general dulness over the chest on percussion. The respiration was chiefly diaphragmatic.

Less than a year before the patient's death Sir William Gull recorded that he was breathless, and had occasional attacks of mental confusion in which he remarked that he could not understand the sense of words. His voice was hoarse and feeble, and the hyoid bone seemed thickened. The head had continued to enlarge, and he maintained that he was still losing in height. The neck was fixed, and somewhat forward. All the viscera appeared normal. The urine, repeatedly examined, was always found normal, and of normal colour.

The record of the post-mortem examination by Dr. Goodhart leaves no doubt that the disease in this case was the same as that which I have described, and it may be important that this patient also had cancerous disease. "A growth . . . corresponding to the growth described as epithelioma of the arachnoid surface of dura mater," grew from the inner surface of the dura mater, was as large as a chestnut and made a pit in the brain near the left Sylvian fissure.

The description of the changed structure of the bones, for which



I may refer to the 'Pathological Transactions,' seems to me to indicate that the disease was more advanced in the direction of degeneracy than that which I have described, or that it had not been in any degree repaired.

CASE 5.—I owe to Mr. Bryant the opportunity of seeing a similar case which was under his care in Guy's Hospital, and of which Mr. Viney was so good as to give me notes.

The patient was a carpenter, sixty years old, a hard-working married man, and had seven children. When about sixteen years old he had a slight attack of gonorrhœa, but without sores, and no history of syphilis could be learned. When thirty-five years old he received an injury to his pelvis. Shortly after this he had trouble with his bladder, which became much distended; a large quantity of clotted blood was washed out. He lay in bed for this six weeks, and at the end of three months was able to go to work again.

For the last five years he had been troubled with gout in his left great toe. His father suffered from this. The attacks had been short; a few days' rest always sufficed for recovery.

About three years before admission he first felt pains of a shooting description about the tendons of the popliteal space, whenever he straightened his legs. At this time also he first noticed a swelling of the legs, which began at the ankles. These symptoms, without his taking any special notice of them, continued for about a year.

In the last year and a half the tibiæ had become much swollen and curved forwards, and on account of the pain he had in them from standing he had been obliged to give up his regular work. Until admission he did not notice anything wrong with his other bones, but he had lost about half an inch in height.

The tibiæ presented a marked curve forwards. The anterior border of each was rounded to a very marked degree, so that it could not be felt at all distinctly. The right tibia was slightly larger than the left. The inner surface of each measured about four inches at its widest part. The veins above the ankle were in a varicose condition.

The fibulæ were very much enlarged; the femora enlarged in their shafts and bowed outwards. The great trochanter was drawn up to the level of a vertical line drawn from the anterior superior spinous process of the ilium to the horizontal line of the body, instead of being about two and a half inches below this line. The patellæ were little larger than natural.

The bones of the upper extremity were enlarged, but not to so marked a degree as those of the lower. The enlargement was most marked in the humeri and the left was thicker than the right. He could not straighten his arms, probably owing to the enlargement of the olecranon. In the clavicles the natural curves were very much increased and the bones thickened, the left more so than the right. In the scapulæ the spines and acromion processes were very much enlarged.

The chest was slightly flattened from side to side, but moved fairly whilst breathing. The ribs on the right side were slightly larger than those on the left.

There was a general curve backwards from the cervical to the dorsal vertebræ, so that the patient's usual position in bed was with his head bent forwards, and his legs in a semi-extended position.

The bones of the hands and feet did not seem to have shared in the general thickening.

There seemed to be a slight thickening about the external protuberance of the occipital bone, but there was no other evidence of the cranial bones being involved.

The patient had cold perspirations over his legs in the evening. His urine had a specific gravity of 1014, was strongly acid, contained a little albumen but no excess of phosphates.

[Six months later Mr. Bryant told me that this patient's bones were still enlarging, and that there were evidences of enlargement of the skull.]

I have looked for records of cases similar to these in nearly every work that seemed likely to contain them, but in vain. I have found only three cases, and the first two of these are doubtful.

Saucerotte\* relates the case of a man who died at forty and in whom all the bones, those of the head, face, orbits, ribs, vertebræ and limbs had begun to enlarge about seven years before death. He increased in weight from 119 livres to 168, wholly from increase of bones; he had rheumatic pains; for a time sleepiness, oppression at the chest, and very small pulse; but these passed-by and he died with some acute illness. No examination was made.

Rullier† tells of a man, aged seventy-eight, who died in the Hôtel Dieu of empyema. He had previously been in good health, and nothing had indicated any derangement of cerebral function. The skull was very large, osteoporotic, and heavy, and, except the lower jaw, all the bones of the face were healthy. The ribs were thicker and larger than usual; the sternum narrow and very thick; the pelvic bones changed like those of the skull. The clavicles were thick, curved, and solid. The other bones were healthy.

Wraný‡ has fully described the condition of the bones in a case of spongy hyperostosis of the skull, pelvis, and left femur, taken from a woman fifty years old, of whom, however, nothing is told but that she died of pyæmia, and that she had "spongy hyperostosis of the skull with atrophy of the facial skeleton, spongy hyperostosis of the vertebral column, pelvis, and left femur, with elongation of the latter bone; kyphoscoliosis of the upper dorsal part of the spine; pelvic abscess; emphysema and œdema of both lungs, abscess of the left; marasmus."

I cannot doubt that this disease was the same as I have here described, and the paper is valuable, both for the many signs indicated in it that the bones softened and yielded to pressure in the early part of the disease, and for the careful comparison of the distortion of the pelvis with the dissimilar distortions in rickets and mollities ossium. The spine was very curved; the chest small and too arched; the whole trunk very short.

From these cases which, though few, are well marked and in some chief points uniform, as well as from a recollection of two

\* 'Mélanges de Chirurgie,' Paris, 1801.

† 'Bulletin de l'École de Médecine de Paris,' t. ii, p. 94, 1812.

‡ 'Prager Vierteljahrschrift,' 1867, B. i, p. 79.

more of which I have no notes, I think we may believe that we have to do with a disease of bones of which the following are the most frequent characters:—It begins in middle age or later, is very slow in progress, may continue for many years without influence on the general health, and may give no other trouble than those which are due to the changes of shape, size, and direction of the diseased bones. Even when the skull is hugely thickened, and all its bones exceedingly altered in structure, the mind remains unaffected.

The disease affects most frequently the long bones of the lower extremities and the skull, and is usually symmetrical. The bones enlarge and soften, and those bearing weight yield and become unnaturally curved and misshapen. The spine, whether by yielding to the weight of the overgrown skull, or by change in its own structures, may sink and seem to shorten with greatly increased dorsal and lumbar curves; the pelvis may become wide; the necks of the femora may become nearly horizontal, but the limbs, however misshapen, remain strong and fit to support the trunk.

In its earlier periods, and sometimes through all its course, the disease is attended with pains in the affected bones, pains widely various in severity and variously described as rheumatic, gouty, or neuralgic, not especially nocturnal or periodical. It is not attended with fever. No characteristic conditions of urine or fæces have been found in it. It is not associated with syphilis\* or any other known constitutional disease, unless it be cancer.

In three out of the five well-marked cases that I have seen or read of cancer appeared late in life; a remarkable proportion, possibly not more than might have occurred in accidental coincidences, yet suggesting careful inquiry.†

\* There has not only been no history of syphilis in any of the cases, but no known syphilitic changes have been observed in any patient.

† See, also, Sandifort, quoted at p. 61; Museum of St. Bartholomew's, ser. i, 111 and 112, sections of a femur, large, curved, porous, with a tumour growing around its shaft; and 49, a hyperostotic skull from a man who died with cancerous disease of the eyeball, heart, and other organs; and Museum of Guy's Hospital, specimens of symmetrical osteoid cancer of the ilia, with cancer of the spine and cranium, associated with hypertrophy of the cranium. Dr. Goodhart was so good as to give me a report of this case.

The bones examined after death show the consequences of an inflammation affecting, in the skull the whole thickness, in the long bones chiefly the compact structure, of their walls, and not only the walls of their shafts but, in a very characteristic manner, those of their articular surfaces.

The changes of structure produced in the earliest periods of the disease have not yet been observed, but it may certainly be believed that they are inflammatory, for the softening is associated with enlargement and with excessive production of imperfectly developed structures, and with increased blood-supply. Whether inflammation in any degree continues to the last, or whether, after many years of progress, any reparative changes ensue, after the manner of a so-called consecutive hardening, is uncertain.

The inflammatory nature of the disease is evident also in the changes of minute structure in the affected bones.\* On these Mr. Butlin writes, "With regard to the nature of the process by which these changes were accomplished, there are probably only three things which could produce so great an increase in the size of a bone, namely, new growth (tumour), hypertrophy, and chronic inflammation.

"The first of these may be at once set aside as out of the question.

"Nor is the second much more probable than the first, for the process is evidently no mere hypertrophy. The whole microscopical architecture of the bone has been altered; the structure appears to have been almost entirely removed and laid down afresh on a different plan and in a larger mould.

"Of the three causes chronic inflammation alone remains, and upon examination one or two facts will be found to bear strongly upon the theory of this being essentially an inflammatory disease. Not only the absorption of the old structure which has taken place but also the manner of this absorption, point to its inflammatory nature. Traces of this are not, of course, always discernible, as the process is almost everywhere far advanced. But still careful observation not uncommonly discovers that the sides of the

\* And this is also the opinion of Wraný, l. c.

widened canals, instead of being smooth and even (Plate III, fig. 10), are eaten out in a series of curves or concavities with the production of what are called Howship's lacunæ, so characteristic of inflammation. The tissue contained in the canals, too, almost precisely resembles the tissue found in the spaces of inflamed bones, only differing from it in being generally more fibrillar and less rich in cells, a fact easily to be accounted for by the very long duration of the disease and the general tendency towards organisation which was displayed throughout. The apparent cessation of the process of absorption and the gradual process of repair may be regarded as still further leading towards the same conclusion.

"Further than this the microscopical observations do not extend."

The chemical analysis by Dr. Russell may be regarded as confirming this conclusion. It shows, at least, that there is no such change of composition in the bone as would be expected in any merely degenerative softening.

Holding, then, the disease to be an inflammation of bones, I would suggest that, for brief reference, and for the present, it may be called, after its most striking character, *Osteitis deformans*. A better name may be given when more is known of it.

It remains that I should point out the distinctions between this disease and the several forms of hyperostosis, osteoporosis, and other diseases among which it has been confused.\*

1. Among cases of hyperostosis are included those of simple overgrowth or hypertrophy of bones in adaptation to increase or change of office. The distinction of these from any form of disease is plain enough; they show a mere increase of natural structure.†

2. Scarcely different from these and as easily distinguished are the hyperostoses, best seen in the skull, in which the bones have more than normal thickness, hardness, and weight, and marks of

\* Many of the statements here made are derived from the examinations of the collections of diseased bones in the College of Surgeons and St. Bartholomew's Hospital, which I made while writing the catalogues of their pathological museums.

† Mus. Coll. Surg., 379, 380, 2838, 2839, 2842, 2843, &c.

greater vascularity, yet preserve a just relation of their several parts and a scarcely changed structure. They probably illustrate the effects of simple inflammation of bone recovered from.\*

3. A group of hyperostoses consists of those cases in which bones are enlarged in consequence of an increased supply of blood of lymph. Such a case is that recorded by Dr. Day† in which the bones of a boy's limb with obstructed lymphatics are much longer than those of the sound limb;‡ and such are all those in which bones near inflamed joints, or with partial necrosis, or in limbs long hyperæmic, from whatever cause, grow in length and circumference till they considerably surpass the bones of the healthy limb.§ These are easily distinguished. They have not signs of disease proper to themselves; they occur in the young alone; they may present a healthy texture, or one only slightly changed as by partaking of the adjacent inflammatory process; and with the exception of the tibia they do not become deformed. The tibia, when it lengthens more than the fibula, is almost compelled to curvature by the fixed unyielding attachment of its ends;¶ and the curve is usually similar in shape and direction to the curve of the tibia in the osteitis deformans. But there is no other likeness between the two conditions.

4. A very large number of cases of hyperostosis are consequences of inflammations of bone; some of simple inflammation, others of scrofulous, syphilitic, or gouty inflammation. It is not necessary here to distinguish these from each other,|| but there are sufficient signs for the distinction of all from the osteitis deformans.

It is clear that the summary which I have given of the clinical characters of this osteitis would not tally with that of any case

\* Mus. Coll. Surg., 2840, 2841.

† 'Transactions of the Clinical Society,' vol. ii, p. 104, 1869.

‡ Broca, 'Des Anévrysmes,' 8vo, p. 76, 1856, gives a case of femoral arterio-venous aneurism attended with considerable elongation of the limb.

§ I believe these were first described by Mr. Stanley, 'On Diseases of Bones,' p. 20, *et seq.*, and myself, 'Lectures on Surgical Pathology,' p. 64, ed. 3, and in the catalogues already referred to. Langenbeck has published a very interesting paper on them in the 'Berliner Klin. Wochenschrift,' 1869, No. 26. Cases are also cited from Weinlechner, Schott, and Bergmann, in Virchow and Hirsch's 'Jahresbericht für 1869.'

¶ Such curved tibiæ are in the museum of St. Bartholomew's, Nos. A. 3, A. 46.

|| An attempt to do so is made in the pathological catalogue of the College of Surgeons.

of simple osteitis, such as might ensue in a healthy person after injury, or in the neighbourhood of a sequestrum; and the clinical difference is as complete between it and any case that could justly be regarded as strumous or syphilitic or gouty osteitis.

The anatomical differences are as well marked: chiefly in the facts that in these inflammations the bones do not become curved\* (unless in the case of the tibia already explained); that they commonly display much more considerable external periosteal outgrowths or deposits, as if from a greater participation of the periosteum in the inflammatory process; that the rarefied or, it may be, porous structure of the swollen shafts of bones usually shows appearances of separation and expansion of the component layers; that the medullary canals are commonly invaded by the thickening walls, or are as much changed as the walls themselves; that the whole length of a bone-shaft is very rarely affected; and that the thin articular layers of bones are, I believe, never thickened as they are in the osteitis deformans.†

It may be added that it is very improbable that any form or degree of scrofula or syphilis or gout should exist in bones or any other textures for ten or more years without affecting other parts and without impairing the general health. The retention of good general health during many years of localised disease is, indeed, one of the most striking characters of the osteitis deformans. The only parallel known to me is in the rheumatoid or chronic rheumatic arthritis, and the likeness between the two in this respect may suggest that they are nearly related; yet they are not found concurrent. In the case that I have related the amount of chronic rheumatic arthritis was trivial, and (which is more important) in all the records and specimens of the arthritis which I have seen I have not found an instance in which there were any of the morbid changes characteristic of the osteitis.‡

5. There are, I think, only two other diseases, namely, rachitis

\* The absence of curving in bones around sequestra is remarkable, for they are long and often acutely inflamed, and those of the lower limbs are commonly used and bear weight.

† Among the specimens in which these changes may be studied are, in the College Museum, Nos. 3085, 3089, 598, 3090, 3091; in the museum at St. Bartholomew's, A. 1, and ser. i, 56, 132, 138, 196-198.

‡ There is not even any mention of them in Mr. R. Adams's elaborate 'Treatise on Rheumatic Gout,' 1873, 8vo and folio.



and osteomalacia, from which it can be necessary to discriminate the osteitis deformans, and the differences between them are very wide. They have scarcely a feature in common except that in all of them the bones bearing weight become curved or misshapen, and the spine is usually deformed, and the skull may become very thick and porous. But in rachitis the bones are too short, not too long; too small, not too large; and their curvatures are quite unlike those of the osteitis. And in the osteomalacia the walls of the bones become exceedingly thin, wasting with an acute atrophy; and when they yield it is not with regular curving but with angular bending or breaking. By these and many other differences, as well clinical as anatomical, the diagnosis of the osteitis from rachitis and osteomalacia is sufficiently clear. With rachitis it may be judged to have no affinity whatever; with osteomalacia only so much as may exist between a chronic inflammation and an acute atrophy of any part. Yet by one character which all these three diseases have or may have in common, namely, the osteoporosis of the skull, they are constantly confounded in museums, if not in practice, with each other, and with diseases different from them all.

The study of the osteitis deformans led me to learn what I could of the various recorded descriptions of large, thick, and porous skulls often found in museums. Nearly every large museum contains one or more specimens of such skulls whole or in fragments. They are all big, thick, porous, or spongy, with obliterated sutures and wide apertures and grooves for blood-vessels. Very few of these specimens have any life-histories; they are all, in many respects, alike and usually are all named alike. Many of them it may be impossible to name or classify without much better knowledge of them than may now be had, but I believe that among them are the results of several different diseases; and it may save some trouble to future students if I refer to some of the specimens and records which have led me to this belief.

1. Some are examples of the osteitis deformans which I have described.\*

\* To those already referred to these, I think, may be added: Sandifort, 'Museum Anat. Acad.,' Lugd.-Bat., fol., 1835, vol. i, p. 142, vol. ii, tab. xiii, Skull of a man forty-three

2. Some are derived from cases of osteomalacia. Mr. Durham\* has written on these, and Mr. Solly's† well-known paper gives a good instance of them. In general, I think that these may be distinguished, at least in the recent state, by their softness and lightness; the abundance of soft medulla contained in them, and the comparative brittleness of the bones when dry.

3. Some are from rachitis; they are, unless after recovery and repair, very light, almost friable, and on their surface not porous, but like fine cloth or felt.‡ Like these are the skulls of some lions and monkeys which have died young, in confinement, of what is considered rickets. A collection of these skulls and other similarly diseased bones in the college museum§ deserves careful study, especially because of their likeness to the cases included in the next group.¶

4. These are the results of a disease of early life, sometimes even of childhood, in which all the bones of the face as well as those of the cranium are affected, and, it is said, the bones of the limbs. All the affected bones, facial as well as cranial (and herein is a clear ground of diagnosis), become hugely thickened, porous, or reticulate. The whole skull is very large, clumsy, and featureless. Commonly the cranial cavity is diminished. The orbital and nasal cavities are contrasted, the antra are often filled, by the ingrowth of their several walls; the apertures for nerves are narrowed or obliterated.||

years old, with a "fungus" over the left orbit (? a cancerous growth). Other similar skulls are here referred to. Similar specimens are, probably, Nos. 2840 and 2858A in the College Museum; and, more uncertainly, 2841 and 2858, which, perhaps, belong rather to the fifth group.

\* 'Guy's Hospital Reports,' ser. iii, vol. x, 1864.

† 'Med. Chir. Trans.,' vol. xxvii, p. 435, Mus. Coll. Surg., 395.

‡ See Mus. Coll. Surg., 390-394, 2844, and 2857. I believe that Huschke, 'Ueber Craniosclerosis,' 1858, quoted by Virchow, contains facts on the rachitic osteoporoses, but I have not been able to refer to it.

§ Nos. 386-388, 2854-2856, 2855A, &c.

¶ Although bones such as these are not described by Paul Gervais, yet his paper quoted below should be studied on all that relates to hyperostosis in animals.

|| Among the casts in the museum at St. Bartholomew's, No. 10, is that of a skull affected with this disease, and in ser. i, 36 are fragments of a bone, which, I think, may be referred to it.

Of these cases, which are among those named by Virchow\* Leontiasis ossea, the best are related by Ilg† and Jadelot.‡ Their descriptions are very scanty, yet they give sufficient facts to distinguish the disease by their account of the cerebral symptoms associated with it. In Ilg's case, for example, the patient who died at twenty-seven, after seventeen years' disease, had amaurosis, epilepsy, severe general headache, delirium, convulsive attacks, and at last total deafness, witlessness, difficulty of swallowing, and loss of smell.

5. Some cases, perhaps not different from these, though they have occurred in later life, are those by Schützenberger,§ Otto¶, and Wraný.||

6. And, lastly, there are cases not so much of thickening of the cranial and facial bones as of enormous bossed and nodular hard bony outgrowths overspreading them or projecting from them. The leading case among these is that published in the 'Transactions' of the Pathological Society by Dr. Murchison,\*\* with a report on the specimens by Mr. De Morgan and Mr. Hulke.†† The disease in which the facial more than the cranial

\* 'Die krankhaften Geschwülste,' B. 11, 1864-5. I need not say that this contains a very complete account of all forms of overgrowth of bone.

† 'Einige Anatomische Beobachtungen,' 4to, Prag, 1821.

‡ Quoted by Ilg from Meckel. The best of many accounts of this specimen is given by Paul Gervais, "De l'hyperostose chez l'homme et chez les animaux," in the 'Journal de Zoologie,' t. iv, 1875. He has carefully reexamined the skull and face and described them.

§ 'Gazette Médicale de Strasbourg,' and in Canstatt's 'Jahresbericht für 1856,' B. iii, 34, with references to cases by Breschet and Nélaton.

¶ Otto, 'Neue seltene Beobachtungen,' 4to, 1824, p. 2. Both head and face are affected; the bones are described as, after softening, very hard, dense, and almost ivory-like. Six hyperostotic skulls are mentioned in his 'Neues Verzeichniss der Anat. Sammlung zu Breslau,' 1841.

|| Wraný, "Hyperostosis maxillarum," in 'Prager Vierteljahrschrift,' 1867, B. 1, similar affections of the facial and cranial bones, with cerebral symptoms. Doubtful cases by Ribelt are quoted by Ilg, l. c.; Malpighi, 'Opera Posthuma,' 4to, Amstel., 1700, p. 68; Kilian, 'Anat. Unters. über den neunten Hirnnervenpaar,' Pesth, 4to, 1822, p. 133; Quekett, reported by Hewett, 'Medical Times and Gazette,' Sept. 8th, 1855, p. 229.

\*\* Vol. xvii, 1866, p. 243.

†† Similar cases are illustrated by Forcade, quoted in Virchow's 'Die krankhaften Geschwülste,' B. 2, p. 22; Weber, from a specimen in the Dupuytren Museum, in v. Pitha and Billroth's 'Handbuch,' B. 3, Abth. 1, Lief ii, p. 257; Howship, 'Practical Observations

bones are affected is clearly distinct from any of the foregoing, or if it be in any way connected with them, especially with those of the fifth group, may be regarded as transitional from them to the exostoses, especially the massive tuberos and bossed ivory exostoses, which grow on or among the bones of the face and skull. The same approach to the character of hard exostoses is shown in the disease of the fibula in Dr. Murchison's case, a section of which, from the museum of the Middlesex Hospital, is now before the Society.

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in *Surgery and Morbid Anatomy*, 1816, p. 26; Adams in *Trans. of the Pathological Society*, vol. xxii, p. 204, 1871; Lysthay, in Canstatt's *Jahresbericht für 1858*; *Mus. Coll. Surg. Eng.*, 3093. Virchow has a full account of nearly all these cases, and of the analogies of the disease with elephantiasis of soft parts.

## DESCRIPTION OF PLATES I TO V

Chronic inflammation of bones (osteitis deformans)

## PLATE I.

Figs. 1-3. From photographs of the patient (Case 1) taken six months before death.

Fig. 4. From photographs of the same patient's cap worn in 1844, and hat worn in 1876.

## PLATE II.

Figs. 1, 2. From tumour of forearm. Fig. 1. Oc. 3, obj. 4.  $\times$  about 62. Fig. 2. Oc. 3, obj. 7. Tube drawn out.  $\times$  260.

Fig. 3. From secondary tumour of pleura. Oc. 3, obj. 7, t. dr. o.  $\times$  260.

Figs. 4, 5. To show tissue in widened canals of tibia (4) and skull (5). Oc. 3, obj. 7, t. d. o.  $\times$  about 260.

Fig. 6. Trabecula of bone (tibia) lined by osteoblasts.  $\times$  about 260.

Figs. 7, 8. From transverse section of tibia. (A. i. in.) Fig. 7 shows new bone growing in periosteum. Fig. 8. Taken from immediately beneath the periosteum.

## PLATE III.

Fig. 9. From perpendicular section of skull. (A. i. in.)

Fig. 10. From section of tibia, to show eaten-out border of widened Haversian canal. Oc. 3, obj. 7.  $\times$  200.

Figs. 11, 12. From transverse section of tibia. Fig. 11. At some distance from surface. Fig. 12. From a little way beneath the periosteum. Oc. 3, obj. 4, t. dr. o.  $\times$  87.

Fig. 13. Transverse section of normal tibia. Oc. 3, obj. 4, t. dr. o.  $\times$  about 87.

PLATE IV.—Upper and lower ends of femur. (College of Surgeons Museum, No. 395B. Half diameter.)

PLATE V.—Cranium. (College of Surgeons Museum, No. 395A. Real size.)

Fig. 1.

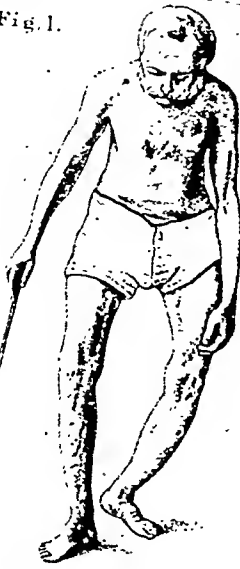


Fig. 2.

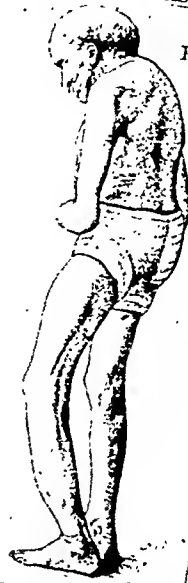
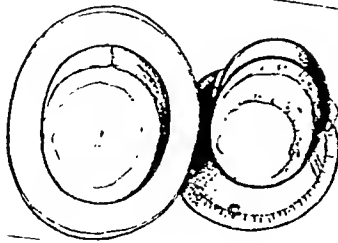


Fig. 3.



Fig. 4.



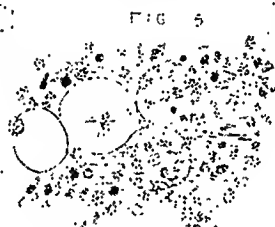


FIG. 9.



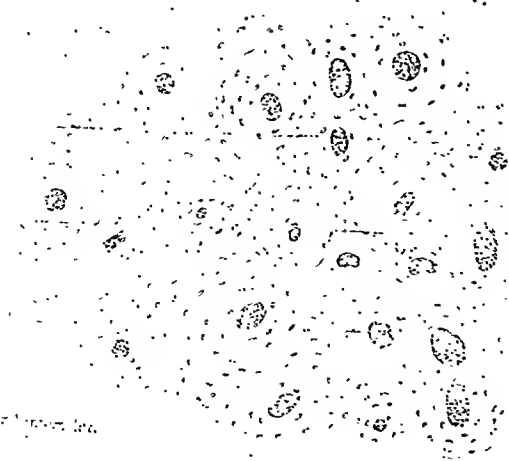
FIG. 10.



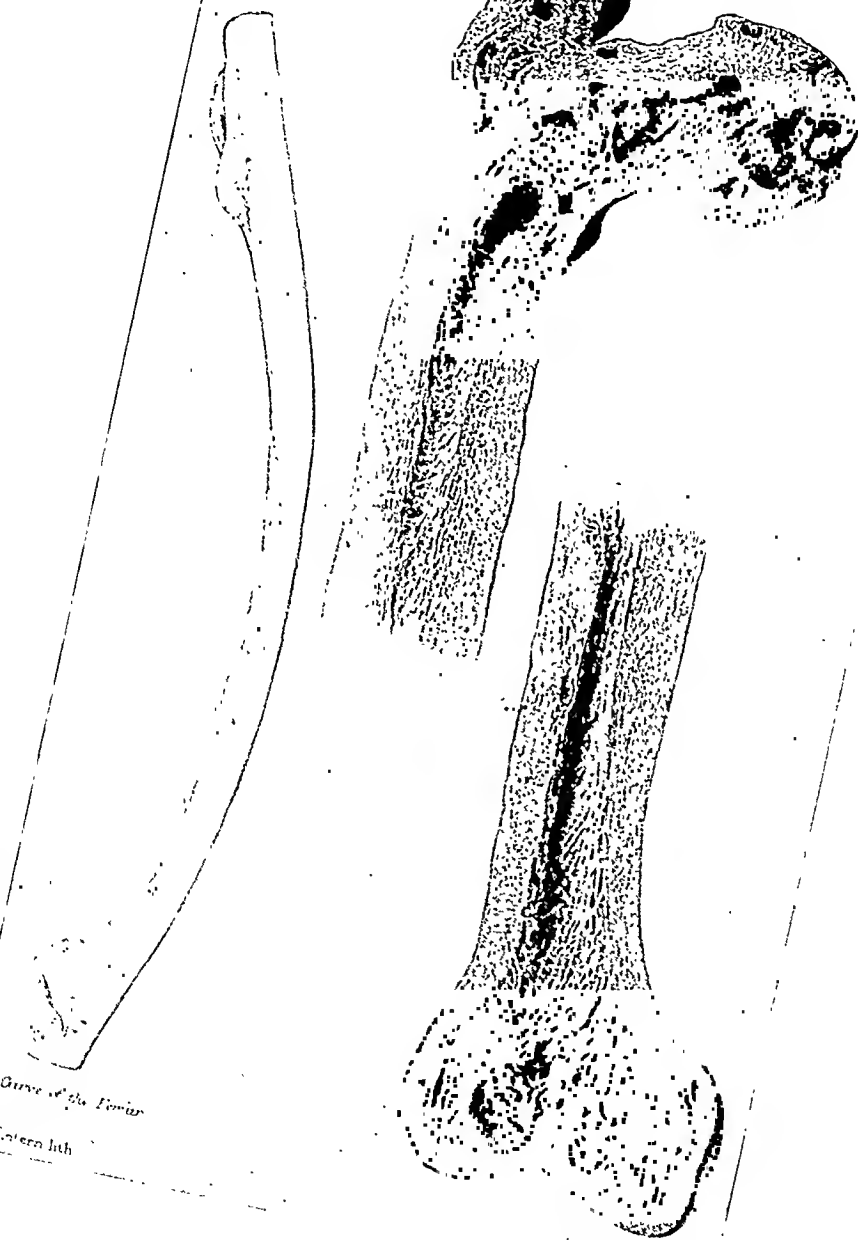
FIG. 11.



FIG. 12.







Curve of the Femur

Western lith

Mintern Bros imp



## ADDITIONAL

# CASES OF OSTEITIS DEFORMANS.

BY

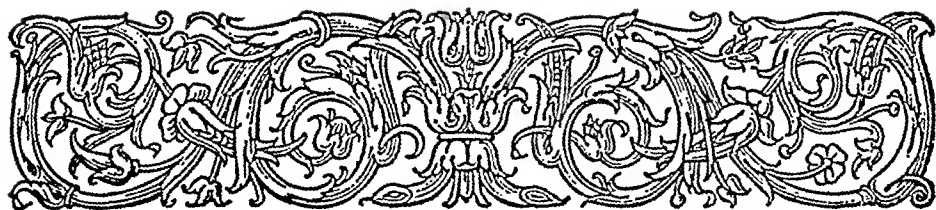
SIR JAMES PAGET, BART., D.C.L., LL.D., F.R.S.,  
SERGEANT SURGEON TO H.M. THE QUEEN, &c.

(Received April 17th—Read June 13th, 1883.)

I SHOULD not have offered to the Royal Medical and Chirurgical Society a mere collection of cases such as this paper contains, if it were not for the hope that they may help to clearly indicate the chief characters of the disease to which I venture to give the name of osteitis deformans, and which, so far as I know, was first described in the paper published in the 60th volume of the Society's 'Transactions.'<sup>1</sup> Since that time, about five years ago,

<sup>1</sup> After the publication of the paper I found that the name osteitis deformans had been given by Prof. Czerny, of Freiburg, to a disease described by him in the 'Wiener medizinische Wochenschrift,' September 27th, 1878. It is mainly, as he says, "Eine lokale Malacie des Unterschenkels," a rather acute inflammation of the lower part of the tibia and fibula, inducing softening and angular bending, and then followed by hardening. A specimen of the only instance of this disease that I have seen has lately been presented to the Museum of the College of Surgeons by Dr. Butt, of Hereford. Like all Prof. Czerny's cases it occurred in a young man.

It may be well to add also that the sternum, a clavicle, and a rib of the man, whose case by Sancerotte is referred to in my last paper, are in the Musée Dupuytren. They were obtained by Sancerotte many years after his account of the case was published. The description of them in the 'Dupuytren Catalogue,' vol. ii, p. 148, leaves it very doubtful whether the disease was osteitis deformans.



# Additional Cases of Osteitis Deformans

BY

SIR JAMES PAGET, BART., D.C.L., LL.D., F.R.S.

*Sergeant Surgeon to H.M. the Queen, &c.*

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CASE I.—May 29th, 1878. A lady, æt. 65, having no appearance of general ill-health and looking her age, complained chiefly of what she deemed to be rheumatic and neuralgic pains of her back and lower limbs. She ascribed them to exposure to cold thirteen years ago; for she had rarely since that time been free from pain, and had lost strength and health; and in the last year or more, had suffered with what she considered to be attacks of bronchitis and asthma.

Soon after the beginning of her pain, that is, about ten or twelve years ago, her daughters thought that she was losing in height, and that the shape of her head was changing; and from that time she had been becoming less tall, till now she had lost four inches and a half in height, and stooped low with her head forward and her chin raised.

She had marks of slight gouty affections in some knotted knuckles, and frequent flatulence and occasional excess of lithic acid in the urine. But she had never had fever, ague, or any acute illness, and had borne five children in rather hard labours, without ill consequences.

Her father had been gouty and died in old age; her mother died young after parturition. She did not know of any case of scrofula, consumption, or cancer having occurred in her family.

Her head, though she said it had always been a remarkably large one, was certainly enlarged, and chiefly by convex bossed additions over and about the junction of the frontal and sagittal sutures and above the temporal sutures. They were symmetrical, and might be guessed to be additions of one third or half an inch in thickness, perhaps additions to a general thickening of the cranium. But they neither were nor had been associated with headache or any other local trouble, and sight, hearing, and the other senses were unimpaired.

The dorsal spine was curved with a very marked posterior rounded curve, inclining a little to the right, without any compensating curve to the left below it. The curve produced a low stooping posture, with very prominent right shoulder, and might be estimated as shortening the trunk about two or two and a half inches.

The ribs were nearly horizontal, flattened at the sides, and, even in deep inspirations, nearly motionless. The respirations were almost wholly diaphragmatic, with elevation of the sternum. They appeared to be sufficient during quietude, but in any hurry or mental emotion, or any unusual exertion, great distress of breathing was felt, and walking upstairs seemed even dangerous; she was always carried up.

The lumbar spine appeared of natural form, so did the pelvis, and likewise all parts of the upper extremities.

The femora were exceedingly curved outwards and forwards; the left rather more than the right. Their shafts felt in their whole length, especially, I think, in their lower half, large, rounded, thickened.

Similarly the tibiæ were curved forwards and were very large in their whole length. Their anterior surfaces felt nearly twice as wide as in nature, smooth, and with large rounded margins.

The feet and all the articulations of the lower limbs appeared quite healthy. None of the enlarged bones were tender on pressure.

The likeness of the forms of the trunk and lower limbs in this case, and in the first case recorded in my former paper, was very striking. The similarity of disease could not be doubted.

The patient lived two years and a half after this note of her case was made, and during this time was under the care of Mr. Haynes, of Stansted, to whom I am indebted for being able to report that little change ensued in the bones of the lower extremities; that the skull became more deformed, especially with a broad, high boss along its upper middle line; and the spine more curved and prominent in its dorsal part. Death ensued in consequence of Bright's disease and valvular disease of the heart, with extreme anasarca. It did not appear due in any degree to the disease of the bones, unless it were that the difficulty of breathing was aggravated by the deformity of the chest. There was no indication of cancerous disease of any part.

Examination after death was not allowed.

CASE 2.—February 17th, 1879. A man, æt. 62, looking in everything but shape completely healthy, and feeling well and

fit for work, even more fit than ever for any mental work, told that he had been healthy all his life, and had been six feet and a half inch high, slim, well made, and active, a volunteer, and given to all kinds of exercise. He was not aware of any unhealthy inheritance, certainly not of gout. He did not know the very beginning of his illness, or any cause for it. He first observed, distinctly, that his stature was less, and that his left limb was rather stiff and lame, in May, 1871, when he was 54. A bone-setter then told him that his hip was "out" and professed to reduce it, and later in the year he was treated for chronic rheumatism at Buxton and obtained there some relief from pain. From this time he appeared to be constantly losing height and becoming more misshapen; but he had never suffered more than might be ascribed to chronic rheumatism of moderate severity in the spine and limbs, and had never left off work or the taking of moderate exercise. He had been obliged to wear larger hats than he had been accustomed to, and had twice or more in the last two years increased the size, but he never had a headache of any kind. Once only in the eight years he had been ill. This was with jaundice, of no great severity, in 1876, and once or twice he had had dyspepsia. Lately he had become rather deaf.

Now he was five feet eight inches, having lost four inches and a half in the eight years. His head was large and well formed, but disproportionate to his face, and his frontal veins looked very full and tortuous. The face was natural. His neck was very short and stiff, and the head was habitually held forward with the chin rather in advance of the sternum, and not more than two inches above it when the face was directed straight forward. The spine was very short, nearly straight, as if its anterior and posterior curves were straightened in the shortening, and it was far too little flexible. The ribs were crowded, nearly horizontal, and hardly raised in inspiration. His inbreathing was almost wholly with the diaphragm, and, when deep, with great uplifting of the shoulders. Yet he called it "pleasant breathing," and was never troubled with it unless on fast walking. The abdomen was short, prominent, overhanging, deeply folded. The clavicles were very big and full-curved, twice as big (at a guess) as they should have been. The arms and hands appeared quite natural, muscular,

and agile, with all the power of writing, fencing, and other uses that they had ever had. I observed nothing wrong in the pelvis. The femora were big and very curved; the left, which had been longer and more affected than the right, was curved outwards and forwards, the right forwards and but little outwards. The tibiæ were big in their whole length, broadly rounded, very curved forward. The feet and all the joints of the lower limbs appeared quite healthy, but the mobility of the hips and knees was lessened.

This patient still lives in fair general health, but with all his deformities increased.

CASE 3.—April 12th, 1879. Mr. M—, æt. 66, formerly a colonial judge, looking older than his years, and dry and rather shrivelled, had had generally good health, but once had fever, and once, about fourteen years ago, congestion of the brain. He had been liable to general rheumatic pains, but not more in the lower limbs than in other parts, and he came for advice about his left ankle, which had become less movable in consequence of the great overhanging of the tibia and the very acute angle in which he habitually held it whilst standing.

His appearance and posture were very characteristic—with his head forward, his shoulders raised, short trunk, legs apart, feet turned out—the right foot forward, the left behind—and both legs greatly curved. Except that he was a shorter and smaller man, the photographs published in the 60th volume of the 'Transactions' might have suited him.

In ten years his height had diminished about two inches, chiefly, I think, from shortening of the spine. The head was well formed and large—it always had been so—and he had always had difficulty in finding a hat large enough for him; but the only indication of increase in it which he had observed was that his present hat was rather tight. The enlargement, however, if any, must have been very little. I could not find any sign of enlargement in the upper limbs. The ribs were nearly horizontal, and less mobile than they should have been. There was less than a finger's breadth between the lowest rib and the crest of the ilium. The spine was not curved below the lower part of the neck. Each



femur in its lower and middle thirds felt thick, and curved forwards and outwards, the right more than the left; the necks of the femora were lowered. The tibiæ were in their whole length very big, rounded at their edges, and exceedingly curved forwards; they felt uneven and knotted, and the integuments in front of them were over-hot; they overhung the feet, and in standing the legs and feet were at acute angles.

The date of the beginning of these changes was uncertain. They had, probably, been in very slow progress for not less than ten years, but they had given so little trouble that they had not been closely watched. No cause of them could be told. One brother was gouty, but the patient himself had not had any marked gout, and had lived a simple temperate life. The disease probably began in Melbourne.

CASE 4.—1880. Mr. S— was 51 years old, a very small man, who had never weighed so much as eight stone, and now was about seven stone eight pounds.

He had so exactly the characteristic form that one could instantly feel sure of the diagnosis of his case. His head was inclined forwards and downwards, his neck looked short, his back was curved backwards, his chest low and small; his pelvis looked broad and womanly; his arms hung low. The lower limbs were arched and divergent: the right advanced, the left as if dropping back, the left foot even more than the right, flat and overhung. The head was, he believed, quite unchanged in size and shape; it was long and flat-sided, but he had not had occasion to change his hat. Both clavicles were enlarged, they felt thick, clumsy, rough. The ribs were very little mobile; the chest was lifted as in one piece when he drew his breath deeply, raising his shoulders. The chest was "square," the ribs flattened at the sides, and bending round with an angle to form the similarly flattened chest front. The ribs severally did not feel as if enlarged. The liver appeared to be pressed high up into the chest; there was dulness to the nipple. The abdomen was wrinkled and undulated as if its walls were too long. The spine was deeply and roundly curved in its dorsal part, but straight in its lumbar. The femora and tibiæ

were very large, especially the lower halves of both, and all were very curved; the femora forwards and outwards, the tibiæ more forwards. The joints felt and looked healthy, but the left knee-joint was painful in movement and rather stiff. Except that he was very thin and dry, all the structures except the bones appeared quite healthy. He could find nothing for complaint but the pain in his knee, which had now lasted some weeks.

He ascribed his illness to a walk down Vesuvius ten years ago. He was very tired with it, was laid up with pains in his lower limbs, and from that time, as he believed, his legs began to curve. Since that time he had not had any considerable illness, but from time to time pains of no great severity confined to the lower limbs. Many years ago he had had syphilis, and there were two scars of tertiary sores on the lower limbs.

I advised him to take iodide of potassium, but it did no good. He remains in good general health and with very slowly progressive changes in his limbs.

In the fifth case, which so far as the notes described, resembled the preceding, Mr. Butlin examined one of the tibiæ post mortem. The condition differed in no degree from that of the bones described in the 60th volume of our 'Transactions.'

CASE 5.—January, 1882. I have so few notes of this next case that I should not have inserted it but for the examination of a portion of one of the diseased tibiæ which Mr. Butlin was so good as to make.

The Rev. Mr. G— had been an active, healthy man, till he was nearly sixty, and he died at sixty-six; his chief signs of illness during this interval having indicated various attacks of irregular gout with bronchitis, emphysema, and diseased heart-valves. He was born of long-lived parents, and had no sign of general disease but such as might be ascribed to gout.

Indications of osteitis deformans had appeared about four years before his death and had slowly increased. The tibiæ especially had gradually become curved forwards, large, rounded, and uneven, and at first had been painful and hot. The femora were also slightly affected, and the spine had become roundly arched and over-hanging at its upper part.

Mr. Butlin reported that the portion of tibia which he minutely examined did not differ in any respect, so far as he could see, from the diseased bones of which his descriptions are recorded in the first case related in my former paper (see vol. lx., p. 46).

CASE 6.—March 9th, 1882. Mrs. S.—, æt. 62, mother of three children, and generally healthy, though with inheritance of gout, and having often flatulence and various gouty symptoms. She was very thin, and her large bossed head, low stooping, and oblique posture, and separated lower limbs, with one far in advance of the other, might at once have sufficed for diagnosis. She believed that her disease began at least ten years ago, when first she observed some enlargement of the external angular processes of the frontal bone. From that time she had had various pains regarded as rheumatic or gouty in her back and lower limbs, and had observed her head growing larger, her spine curving, her height diminishing, her lower limbs bending and becoming weaker, till now she was nearly four inches shorter than she used to be, could hardly stand without support, and walked slowly and as if her right leg were too long.

Her head appeared enlarged at every part, and measured twenty-four inches in its largest circumference; it had a square look, and was bossed, chiefly over the frontal and parietal protuberances and over the lower part of the occiput. The orbital arches also appeared large and prominent, but in the bones of the face there was no apparent change. The dorsal part of the spine was very curved backwards and to the right, the chest was shortened, the ribs crowded but fairly movable. The pelvis seemed not changed. The clavicles were very large and curved, like those of a strong man, contrasting strangely with the thin weak look of the upper limbs, whose bones were slim and naturally straight.

Both femora and both tibiæ were very curved forwards and outwards, and felt large and rugged. Especially the lower parts of the tibiæ were enlarged, and there was little diminution of size between the shafts and the articular ends, which seemed as if over-hanging the ankles. Both shins felt hot.

The bones of both hands and feet were healthy unless for some nodular enlargement of the phalanges such as one sees due to gout.

The patient was not aware of any inherited liability except that of gout, or of anything that could have induced the disease of bones. She had never been dangerously ill.

Lately her sight had become much impaired and still more lately she had been becoming deaf.

CASE 7.—May, 1882. In this case, a lady, *æt.* 58, presented the usual characters of the disease in a well-marked form, but had observed the first signs of it when she was only 28. At that time, during the fatigue of long nursing a relative, she had pains in her lower limbs and found her tibiæ becoming large and curved. Her spine also at this time began to curve. The disease was very slowly and almost painlessly progressive; its chief or only seats being the tibiæ, femora, spine, and clavicles; but when she was 53 she observed enlargement and slight curvature in the lower thirds of both radii. She ascribed this to the exertions she used in frequently lifting her invalid husband, and the morbid changes had continued slowly increasing ever since. Her head was very large, measuring twenty-four inches and a half in its greatest circumference, and looking as if unnaturally prominent in the middle and upper frontal part, but she was sure that this was only its natural size and shape.

With the exception of the disease of the bones and the consequent great difficulty of walking, this lady seemed in excellent health. She had lived very actively; had had two children without any ill consequences, and knew of no inherited tendency to disease unless it were to gout. She had had various treatment with both baths and medicines, but none had seemed useful even for a time.

The seven cases now related seem sufficient when added to the five recorded in the 60th volume, to justify the giving of a distinctive name and a definite general description of the disease observed in them. It usually affects many bones, most frequently the long bones of the lower extremities, the clavicles, and the vault of the skull. The affected bones become enlarged and

heavy, but with such weakening of their structure that those which have to carry weight or to bear much muscular traction become unnaturally curved and misshapen. The disease is very slowly progressive, and is felt only in pain, like that of rheumatism or neuralgia, in the affected limbs, and in increased heat at the *tibiæ*. But neither the pain nor the heat are constant, nor do they continue during the whole progress of the disease; and pain has not been observed in the head even in the cases in which the skull was very thickened. There is not any clear evidence of general disturbance of health. In all the cases traced to the end of life, death has ensued through some coincident, not evidently associated, disease, which has been aggravated by the condition of the bones only in so far as they may have diminished the range of breathing and the general muscular activity.

At present, with the exception of the seventh case, this disease has been observed as beginning only in persons over forty years old, and it has appeared in no usual relation, whether by inheritance or coincidence, with any other disease except gout. I have not found cases to be added to those mentioned in my last paper in which it was associated with cancer.

In all the cases I have seen, the general appearance, postures, and movements of the patients have been so alike that these alone might often suffice for diagnosis of the disease. The most characteristic are the loss of height indicated by the low position of the hands when the arms are hanging down; the low stooping, with very round shoulders and the head far forwards, and with the chin raised as if to clear the upper edge of the sternum; the chest sunken towards the pelvis, the abdomen pendulous; the curved lower limbs, held apart and usually with one advanced in front of the other, and both with knees slightly bent; the ankles overhung by the legs, and the toes turned out. The enlarged cranium, square looking or bossed, may add distinctiveness to these characters, and they are completed in the slow and awkward gait of the patients, and in the shallow costal breathing, compensated by wide movements of the diaphragm and abdominal wall, and in deep breathing by the uplifted shoulders.

I have seen no case in which these characters are imitated except

those of ankylosis of the vertebræ and ribs, to which I referred in my last paper, and which have been described by Dr. Allen Sturge<sup>1</sup> under the name of spondylitis deformans; but these are easily distinguished by the lower limbs being naturally straight and the clavicles and skull unchanged.

<sup>1</sup> 'Trans. of the Clinical Society,' xii, p. 204, 1879.



## PAGET'S DISEASE OF THE NIPPLE

When 60 years of age and consulting surgeon to St. Bartholomew's Hospital, Sir James Paget published a short paper in the Reports of that institution, Vol. X, 1874. This essay, *Disease of the mammary areola preceding cancer of the mammary gland*, contains only 1050 words but the condition is still known as Paget's disease of the nipple and has given rise to a long, still-unsettled controversy on the true nature of the process. See the following pages for the complete paper. For brevity and value this article compares favorably with Colles's paper on fracture of the radius which contains only 1528 words.

Many physicians believe that dermatitis of the nipple preceding cancer of the breast was described by Velpeau in 1840 but the condition was not isolated as a distinct disease until Paget's description in 1874. Since then many cases have been reported, Deaver and McFarland having collected about 300 in 1917. Their book, *The Breast, Its Anomalies, Its Diseases and Their Treatment*, Phila., Blakiston, contains an admirable review of the history of the condition and is the source of many of these notes.

All the cases Paget described were not of the same clinical nature as far as the dermatitis presented itself but all these cases were followed by cancer within two years. Because Paget gave no histo-pathologic description, much confusion has arisen as to what cases should be included under his name. Today a definite histologic picture is recognized, consisting of "epithelial hypertrophy, subepithelial round-cell infiltration and Paget's cells" (Kilgore, A. R., Arch. Surg., 3: 324-335, 1921). Paget's cells should not be called by his name, as he did not describe them, but they form a characteristic feature of the condition. They are large edematous cells in the epithelium, vacuolated, with shrunken, pyknotic nuclei, and are not neoplastic.

There are four chief opinions regarding Paget's disease: (1) that it is a dermatitis or eczema of the skin; (2) that it is a primary squamous-cell epithelioma of the skin; (3) that it is a carcinoma developing from the lactiferous ducts in the nipple and sudoriferous ducts of the skin, secondarily involving the skin and breast tissue; and (4) that it is a carcinoma beginning deep in the tissue of the breast and growing up along the ducts of the nipple and finally invading the skin. (Caylor, H. D., Surg. Clin. No. Amer., 9: 951-956, 1929.)

An interesting group of cases of extramammary Paget's disease has also been reported. This disposes of opinion number four just quoted, but J. F. Fraser considers the majority of such cases as examples of mistaken diagnoses and the others as sweat duct cancers (N. Y. State Jour. Med., 30: 13-15, 1930). He concludes that Paget's disease of the nipple is a mild grade of carcinoma of the intraepidermal portion of the mammary duct.

Since Paget's original description included a variety of cases, we are privileged to apply his name to many different clinical forms of malignant papillary dermatitis. If too many, seemingly unrelated or ill-defined cases are described under this great surgeon's name, we can only say that the explanation may be our great ignorance of the true nature of cancer. Paget recognized, just 60 years ago, the one constant factor in the mystery of cancer that we know today, namely, chronic irritation and he also held the modern view toward hereditary susceptibility.



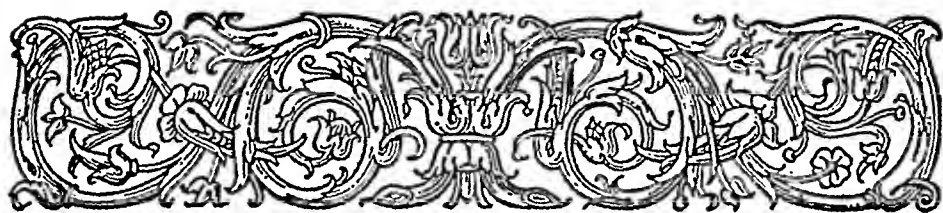
ON  
DISEASE OF THE MAMMARY AREOLA  
PRECEDING  
CANCER OF THE MAMMARY GLAND.

BY  
SIR JAMES. PAGET, BART.; F.R.S.

I believe it has not yet been published that certain chronic affections of the skin of the nipple and areola are very often succeeded by the formation of scirrhus cancer in the mammary gland. I have seen about fifteen cases in which this has happened, and the events were in all of them so similar that one description may suffice.

The patients were all women, various in age from 40 to 60 or more years, having in common nothing remarkable but their disease. In all of them the disease began as an eruption on the nipple and areola. In the majority it had the appearance of a florid, intensely red, raw surface, very finely granular, as if nearly the whole thickness of the epidermis were removed; like the surface of very acute diffuse eczema, or like that of an acute balanitis. From such a surface, on the whole or greater part of the nipple and areola, there was always copious, clear, yellowish, viscid exudation. The sensations were commonly tingling, itching, and burning, but the malady was never attended by disturbance of the general health. I have not seen this form of eruption extend beyond the areola, and only once have seen it pass into a deeper ulceration of the skin after the manner of a rodent ulcer.

In some of the cases the eruption has presented the characters of an ordinary chronic eczema, with minute vesications, succeeded



# On Disease of the Mammary Areola Preceding Cancer of the Mammary Gland

BY

SIR JAMES PAGET, BART., F.R.S.

**I** BELIEVE it has not yet been published that certain chronic affections of the skin of the nipple and areola are very often succeeded by the formation of scirrhus cancer in the mammary gland. I have seen about fifteen cases in which this has happened, and the events were in all of them so similar that one description may suffice.

The patients were all women, various in age from 40 to 60 or more years, having in common nothing remarkable but their disease. In all of them the disease began as an eruption on the nipple and areola. In the majority it had the appearance of a florid, intensely red, raw surface, very finely granular, as if nearly the whole thickness of the epidermis were removed; like the surface of very acute diffuse eczema, or like that of an acute balanitis. From such a surface, on the whole or greater part of the nipple and areola, there was always copious, clear, yellowish, viscid exudation. The sensations were commonly tingling, itching, and burning, but the malady was never attended by disturbance of the general health. I have not seen this form of eruption extend beyond the areola, and only once have seen it pass into a deeper ulceration of the skin after the manner of a rodent ulcer.

In some of the cases the eruption has presented the characters

of an ordinary chronic eczema, with minute vesications, succeeded by soft, moist, yellowish scabs or scales, and constant viscid exudation. In some it has been like psoriasis, dry, with a few white scales slowly desquamating; and in both these forms, especially in the psoriasis, I have seen the eruption spreading far beyond the areola in widening circles, or, with scattered blotches of redness, covering nearly the whole breast.

I am not aware that in any of the cases which I have seen the eruption was different from what may be described as long-persistent eczema, or psoriasis, or by some other name, in treatises on diseases of the skin; and I believe that such cases sometimes occur on the breast, and after many months' duration are cured, or pass by, and are not followed by any other disease. But it has happened that in every case which I have been able to watch, cancer of the mammary gland has followed within at the most two years, and usually within one year. The eruption has resisted all the treatment, both local and general, that has been used, and has continued even after the affected part of the skin has been involved in the cancerous disease.

The formation of cancer has not in any case taken place first in the diseased part of the skin. It has always been in the substance of the mammary gland, beneath or not far from the diseased skin, and always with a clear interval of apparently healthy tissue.

In the cancers themselves, I have seen in these cases nothing peculiar. They have been various in form; some acute, some chronic, the majority following an average course, and all tending to the same end; recurring if removed, affecting lymph-glands and distant parts, showing nothing which might not be written in the ordinary history of cancer of the breast.

The single noteworthy fact found in all these cases is that which I have stated in the first sentence, and I think it deserves careful study. For the sequence of cancer after the chronic skin-disease is so frequent that it may be suspected of being a consequence, and must be always feared, and may be sometimes almost certainly foretold. I believe that a nearly similar sequence of events

may be observed in other parts. I have seen a persistent "rawness" of the glans penis, like a long-enduring balanitis, followed after more than a year's duration by cancer of the substance of the glans. A chronic soreness or irritation (of whatever kind) on the surface of the lower lip often long precedes cancer in its substance; and, with a frequency surpassing all other cases of the kind, the superficial syphilitic diseases of the tongue are followed, and not superseded, by cancers which do not always appear to commence in a diseased part of the tongue.

For an explanation of these cases it may be suggested that a superficial disease induces in the structures beneath it, in the course of many months, such degeneracy as makes them apt to become the seats of cancer; and that this is chiefly likely to be observed in the cases of those structures which appear to be, naturally, most liable to cancer, as the mammary gland, the tongue, and the lower lip. One may suspect that similar surface-irritation has much to do with the frequency of cancer of the rectum, pylorus, and ileo-cæcal valve, in any of which parts the degeneracy, which might come naturally in old age and make them apt for cancer, may be hastened, and made prematurely sufficient, by an adjacent disturbance of nutrition.

In practice, the question must be sometimes raised whether a part through whose disease or degeneracy cancer is very likely to be induced should not be removed. In the member of a family in which cancer has frequently occurred, and who is at or beyond middle age, the risk is certainly very great that such an eruption on the areola as I have described will be followed within a year or two by cancer of the breast. Should not, then, the whole diseased portion of skin be destroyed or removed as soon as it appears incurable by milder means? I have had this done in two cases, but, I think, too late. Or, again, when one with a marked family-liability to cancer has syphilitic disease of the mucous membrane of the tongue, with frequent recurrences of inflammation, should not all the worst pieces of the membrane be removed? I should certainly advise it, especially if the membrane were ichthyotic, if it were not that the disease is commonly

so extensive that good scar-tissue would not be likely to be formed, and that bad scar-tissue, often irritable and ulcerating, is as likely to induce cancer as the syphilitic or ichthyotic patches would have been.

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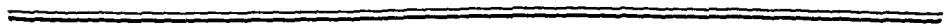
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SIR CHARLES BELL, AET. 30

Painted by Anthony Stewart, Edinburgh, 1804. Reproduced from The Johns Hopkins Hospital Bulletin, Vol. 21, June, 1910

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## Sir Charles Bell

Scotch Physiologist, Physician and Surgeon  
in London, 1774-1842

### BIOGRAPHY

- 1774 Born in November, a son of William Bell and Margaret Morice, daughter of Bishop White. William Bell was a clergyman in the Episcopal Church of Scotland and had dedicated his son Charles to the medical profession in gratitude for relief at the hands of a surgeon.
- 1779 Age 5. Father died. Received education from mother and brothers; was taught French and drawing at home.
- 1785 Age 11. Had to give up school because of financial strain on family although the cost was only five shillings a quarter. Later attended high school for two years which he says he did not like, but from later writings we see he must have been proficient in Latin. Had great artistic talent. Later attended the University of Edinburgh two years before he thought seriously of taking up medicine.
- 1797 Age 23. While a medical student began *System of Dissections*. Trained under Monroe, the second, an able teacher.
- 1799 Age 25. Graduated. On August 1st became a Fellow of the Royal College of Surgeons of Edinburgh and thus a member of the surgical staff of the Royal Infirmary.
- 1800 Age 26. Left in charge of extramural school in Edinburgh

by his brother John; had to accept not only work but John's quarrels and thus found his way in Edinburgh barred; in 1804 excluded from hospital, others getting appointment by seniority.

- 1804 Age 30. Went to London where he was badly received by Mr. Carlisle at Westminster Hospital but befriended by Carlisle's colleague, Mr. Lynn, a Scot. Instituted private lectures.
- 1805 Age 31. While waiting for patients rode out with Abernethy, and dined with Sir Joseph Banks and Dr. Mathew Baillie.
- 1806 Age 32. Took Speaker Anslow's house in Leicester Square with \$60 in pocket; gave opening lecture on a wet night in January. 40 attended but only 12 enrolled. Disappointed. Wrote *Anatomy of Expression*.
- 1809 Age 35. Went to Portsmouth to study gun-shot injuries in the wounded from the battle of Corunna. Still chiefly interested in anatomy rather than surgery. Made many fine drawings and paintings of cases.
- 1811 Age 37. Married Marion Shaw of Ayr. Moved into house at 34 Soho Square. The house pupils, though few, were not welcome to Mrs. Bell. He wrote his brother, "You must consider that these young men are house pupils, not boarders. Dr. Denman, Dr. Baillie, Mr. Hunter, Abernethy, Cooper, Wilson have had them or have them. Their necessity is understood, they are admitted as being essential to a lecturer." Published *Idea of a New Anatomy of the Brain*. Then there "was an awful pause in regard to patients."
- 1813 Age 39. Admitted to Royal College of Surgeons.
- 1815 Age 41. In busy practice. Visited fields of Waterloo after the battle and laboured with the French surgeons at Bruxelles. A portrait, now in the National Gallery, shows him at this time dressed in white waistcoat and green coat, wearing his hair short and without powder, a true dandy. From his wife's letter we read he was "dressing himself young."

- 1827 Age 53. Aided in founding University College, London.
- 1829 Age 55. Awarded first annual medal given by George IV for discoveries in science by Royal Society of London.
- 1830 Age 56. Received Guelphic Order of Knighthood when William IV ascended throne of England.
- 1835 Age 61. Took active part in founding medical school of Middlesex Hospital.
- 1836 Age 62. Left London after living there thirty-two years, during which time he wrote faithfully to his brother George, Professor of Law of Scotland in University of Edinburgh. These letters have been published. Returned to Edinburgh, city of birth, and was Professor of Surgery in the University of Edinburgh, his Alma Mater, until 1842.
- 1840 Age 66. Visited Italy. Fishing became a hobby.
- 1842 Age 68. Died suddenly of coronary thrombosis at Hallow Park, near Worcester, April 29. Buried in churchyard.

Bell's collection of anatomical dissections, comprising normal and pathologic anatomy, human and comparative, second only to John Hunter's collection, is now owned by the Royal College of Surgeons of Edinburgh.

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2. NERVE: The external respiratory nerve. *On the nerves; giving an account of some experiments on their structure and functions, which lead to a new arrangement of the system*. Phil. Trans. Roy. Soc. Lond., 111: 398-424, 1821. Also: *The Nervous System of the Human Body*. Washington, D. Green, 1833, p. 39.
3. PALSY: Facial paralysis. *On the nerves; giving an account of*

*some experiments on their structure and functions, which lead to a new arrangement of the system.* Phil. Trans. Roy. Soc. Lond., 111: 398-424, 1821. See 2. Nerve. *On the nerves of the face; being a second paper on that subject.* Ibid., 119: 317-330, 1829. Also: *The Nervous System of the Human Body.* Washington, D. Green, 1833, p. 59.

4. PHENOMENON: An outward and upward rolling of the eyeball on an attempt to close the eye, occurring on the affected side in peripheral facial (Bell's) palsy. *On the motions of the eye, in illustration of the uses of the muscles and nerves of the orbit.* Phil. Trans. Roy. Soc. Lond., 113: 166-186, 1823. Also: *The Nervous System of the Human Body.* Washington, D. Green, 1833, p. 101.
5. SIGN: See phenomenon.

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## BELL'S LAW OF PHYSIOLOGY OF NERVES

(Anterior roots of spinal nerves are motor, posterior are sensory)

As Harvey is credited with the discovery of circulation of the blood, Aselius of Pavia and Pecquet with the discovery of the function of lacteals and Rudbeck and Bartolene with Hunter and Monro with the discovery of the function of lymphatics, so Sir Charles Bell is credited with the discovery of the function of different types of nerves. Before Harvey there was thought to be an ebb and flow "backwards and forwards like the tide of Euripus" in the blood vessels. In like manner before Bell it was taught that the same nerves "transmitted the mandate of the will from the sensorium to the organs of voluntary motion, and likewise carried to the sensorium intelligence of the condition of their extremities or sensation." The same nerve might transmit, in some mysterious manner, messages in both directions at the same time. We certainly cannot smile at this idea for even today we do not know the true nature of a nervous impulse.

There had been many questions raised throughout the centuries by anatomists and particularly by physiologists as to the true function of the nerves. Galen (131-201 A.D.) is said to have noticed that a limb which had lost its power of motion still remained sensitive and questioned from this fact if there might not be two different types of nerves. Boerhaave (1668-1738) asserted his belief that two kinds of spinal nerves existed—one for motion, the other for senses. But he did nothing to prove his belief was correct and the old theory was still popular. Haller (1708-1777) investigated the subject but stated, "I know not a nerve which has sensation without also producing motion. . . ." Bichat (1771-1802) asserted that there are no nerves exclusive for sensation or for motion. Cuvier (1769-1832) wrote that the difference in the functions of nerves depends on the tissue at the point of distribution or innervation rather than on any difference in the nerves themselves. (See modern experiments on regeneration of nerves by Langley in *Journal of Physiology*, 1899 and 1904.)

Alexander Monro (secundus) (1737-1817), a teacher of Charles Bell, combated the theory that ganglia were for the purpose of cutting off sensation, on the express ground that they were to be found on the posterior half of all the spinal nerves of the voluntary muscles; thus showing that, to be a nerve of voluntary motion, was by him regarded as conclusive evidence that it must also be a nerve of sensation, and that he believed all those spinal nerves which passed through ganglia to be motor nerves (M'Neill).

Bell's discovery of the function of nerves should be considered as epoch making as Harvey's discovery of the circulation. The latter had many prediscovered facts, such as the lesser circulation and the valves in veins, to place him on the right track; these do not detract from his ability to solve the puzzle and prove his theory. But Bell seems to have inherited very few facts from his professional predecessors which aided him in proving his beliefs correct. We must give credit to his genius, his steadfast holding to ideas and to his tireless energy in experimentation and writing.

The following letters show Bell's own attitude toward his work:

November 26, 1807, to his brother—"... I have done a more interesting nova anatomia cerebri humani than it is possible to conceive. I lectured on it yesterday. I prosecuted it last night till one o'clock, and I am sure it will be well received. . . ."

November 30, 1807, "... I really think this new Anatomy of the Brain will strike more than the discovery of the lymphatics being absorbents. . . ."

London, December 5, 1807, to his brother, Professor George Joseph Bell, "... My new Anatomy of the Brain is a thing which occupies my head almost entirely. I hinted to you formerly that I was "burning," or on the eve of a grand discovery. I consider the organs of the outward senses as forming a distinct class of nerves from the others. I trace them to corresponding parts of the brain totally distinct from the origin of the others. I take five tubercles within the brain as the internal senses. I trace the nerves of the nose, eye, ear, and tongue to these. Here I see established connections. Then the great mass of the brain receives processes from these central tubercles. Again the greater mass of the cerebrum sends down processes or crura, which give off all the common nerves of voluntary motion, etc. I establish thus a kind of circulation, as it were. In this enquiry I describe many new connections. The whole opens up in a new and simple light; the nerves take a simple arrangement; the parts have appropriate nerves; and the whole accords with the phenomena of the pathology, and is supported by interesting views. . . . My object is not to publish this, but to lecture it . . . as it is really the only new thing that has appeared in anatomy since the days of Hunter; and, if I make it out, as interesting as the circulation, or the doctrine of absorption. But I must still have time. . . ."

Many workers who followed Bell recognized the value of his teaching and writing and gave him credit for his original discoveries. Bell's brother-in-law, John Shaw, assisted in the work manually and mentally. Herbert Mayo, a pupil, later gave confirmation to the same experiments. On the Continent, Loujet, Bellingeri and Magendie are notable for following the same line and arriving at the same conclusions. All these men gave credit to Bell for the original work; especially Magendie, whose name is often linked with Bell in the history of physiology of nerves, acknowledged in 1822-1823 Bell's priority of discovery. But to Magendie is given the honor of advancing further than Bell in demonstrating and correctly interpreting the functions of both motor and sensory roots.

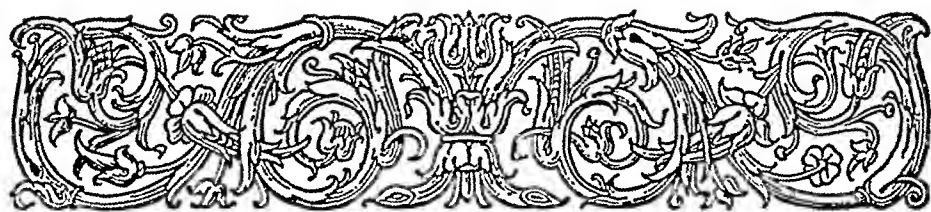
The book here reproduced was published in London in 1811, a copy being in the Surgeon General's Library, but none in the New York State or New York Academy of Medicine Libraries. It was considered so historically important that Sudhoff made it No. 13 of his *Klassiker der Medizin*, Leipzig, 1911, in original English and German translation.



**I D E A**  
**OF**  
**A NEW ANATOMY**  
**OF THE**  
**B R A I N;**

**SUBMITTED**  
**FOR THE OBSERVATIONS OF HIS FRIENDS;**

**BY**  
**CHARLES BELL, F.R.S.E.**



# Idea of a New Anatomy of the Brain

BY

CHARLES BELL, F.R.S.E.

## NOTE



THE want of any consistent history of the Brain and Nerves, and the dull unmeaning manner which is in use of demonstrating the brain, may authorize any novelty in the manner of treating the subject.

I have found some of my friends so mistaken in their conception of the object of the demonstrations which I have delivered in my lectures, that I wish to vindicate myself at all hazards. They would have it that I am in search of the seat of the soul; but I wish only to investigate the structure of the brain, as we examine the structure of the eye and ear.

It is not more presumptuous to follow the tracts of nervous matter in the brain, and to attempt to discover the course of sensation, than it is to trace the rays of light through the humours of the eye, and to say, that the retina is the seat of vision. Why are we to close the investigation with the discovery of the external organ?

It would have been easy to have given this Essay an imposing splendour, by illustrations and engravings of the parts, but I submit it as a sketch to those who are well able to judge of it in this shape.

The prevailing doctrine of the anatomical schools is, that the whole brain is a common sensorium; that the extremities of the

nerves are organized, so that each is fitted to receive a peculiar impression; or that they are distinguished from each other only by delicacy of structure, and by a corresponding delicacy of sensation; that the nerve of the eye, for example, differs from the nerves of touch only in the degree of its sensibility.

It is imagined that impressions, thus differing in kind, are carried along the nerves to the sensorium, and presented to the mind; and that the mind, by the same nerves which receive sensation, sends out the mandate of the will to the moving parts of the body.

It is further imagined, that there is a set of nerves, called vital nerves, which are less strictly connected with the sensorium, or which have upon them knots, cutting off the course of sensation, and thereby excluding the vital motions from the government of the will.

This appears sufficiently simple and consistent, until we begin to examine anatomically the structure of the brain, and the course of the nerves,—then all is confusion: the divisions and subdivisions of the brain, the circuitous course of nerves, their intricate connections, their separation and re-union, are puzzling in the last degree, and are indeed considered as things inscrutable. Thus it is, that he who knows the parts the best, is most in a maze, and he who knows least of anatomy, sees least inconsistency in the commonly received opinion.

In opposition of these opinions; I have to offer reasons for believing, That the cerebrum and cerebellum are different in function as in form; That the parts of the cerebrum have different functions; and that the nerves which we trace in the body are not single nerves possessing various powers, but bundles of different nerves, whose filaments are united for the convenience of distribution, but which are distinct in office, as they are in origin from the brain:

That the external organs of the senses have the matter of the nerves adapted to receive certain impressions, while the corresponding organs of the brain are put in activity by the external excitement: That the idea or perception is according to the part of the brain to which the nerve is attached, and that each organ

has a certain limited number of changes to be wrought upon it by the external impression:

That the nerves of sense, the nerves of motion, and the vital nerves, are distinct through their whole course, though they seem sometimes united in one bundle; and that they depend for their attributes on the organs of the brain to which they are severally attached.

The view which I have to present, will serve to shew why there are divisions, and many distinct parts in the brain: why some nerves are simple in their origin and distribution, and others intricate beyond description. It will explain the apparently accidental connection between the twigs of nerves. It will do away the difficulty of conceiving how sensation and volition should be the operation of the same nerve at the same moment. It will shew how a nerve may lose one property, and retain another; and it will give an interest to the labours of the anatomist in tracing the nerves.

#### IDEA, &c.

When in contemplating the structure of the eye we say, how admirably it is adapted to the laws of light! we use language which implies a partial, and consequently an erroneous view. And the philosopher takes not a more enlarged survey of nature when he declares how curiously the laws of light are adapted to the constitution of the eye.

This creation, of which we are a part, has not been formed in parts. The organ of vision, and the matter or influence carried to the organ, and the qualities of bodies with which we are acquainted through it, are parts of a system great beyond our imperfect comprehension, formed as it should seem at once in wisdom; not pieced together like the work of human ingenuity.

When this whole was created, (of which the remote planetary system, as well as our bodies, and the objects more familiar to our observation, are but parts,) the mind was placed in a body not merely suited to its residence, but in circumstances to be moved by the materials around it; and the capacities of the mind, and the powers of the organs, which are as a medium betwixt

the mind and the external world, have an original constitution framed in relation to the qualities of things.

It is admitted that neither bodies nor the images of bodies enter the brain. It is indeed impossible to believe that colour can be conveyed along a nerve; or the vibration in which we suppose sound to consist can be retained in the brain: but we can conceive, and have reason to believe, that an impression is made upon the organs of the outward senses when we see, or hear, or taste.

In this inquiry it is most essential to observe, that while each organ of sense is provided with a capacity of receiving certain changes to be played upon it, as it were, yet each is utterly incapable of receiving the impressions destined for another organ of sensation.

It is also very remarkable that an impression made on two different nerves of sense, though with the same instrument, will produce two distinct sensations; and the ideas resulting will only have relation to the organ affected.

As the announcing of these facts forms a natural introduction to the Anatomy of the Brain, which I am about to deliver, I shall state them more fully.

There are four kinds of Papillæ on the tongue, but with two of those only we have to do at present. Of these, the Papillæ of one kind form the seat of the sense of taste; the other Papillæ (more numerous and smaller) resemble the extremities of the nerves in the common skin, and are the organs of touch in the tongue. When I take a sharp steel point, and touch one of *these* Papillæ, I feel the sharpness. The sense of *touch* informs me of the shape of the instrument. When I touch a Papilla of taste, I have no sensation similar to the former. I do not know that a point touches the tongue, but I am sensible of a metallic taste, and the sensation passes backward on the tongue.

In the operation of couching the cataract, the pain of piercing the retina with a needle is not so great as that which proceeds from a grain of sand under the eyelid. And although the derangement of the stomach sometimes marks the injury of an organ so delicate, yet the pain is occasioned by piercing the

outward coat, not by the affection of the expanded nerve of vision.

If the sensation of light were conveyed to us by the retina, the organ of vision, in consequence of that organ being as much more sensible than the surface of the body as the impression of light is more delicate than that pressure which gives us the sense of touch; what would be the feelings of a man subjected to an operation in which a needle were pushed through the nerve. Life could not bear so great a pain.

But there is an occurrence during this operation on the eye, which will direct us to the truth: when the needle pierces the eye, the patient has the sensation of a spark of fire before the eye.

This fact is corroborated by experiments made on the eye. When the eye-ball is pressed on the side, we perceive various coloured light. Indeed the mere effect of a blow on the head might inform us, that sensation depends on the exercise of the organ affected, not on the impression conveyed to the external organ; for by the vibration caused by the blow, the ears ring, and the eye flashes light, while there is neither light nor sound present.

It may be said, that there is here no proof of the sensation being in the brain more than in the external organ of sense. But when the nerve of a stump is touched, the pain is as if in the amputated extremity. If it be still said that this is no proper example of a peculiar sense existing without its external organ, I offer the following example: *Quando penis glandem exedat ulcus, et nihil nisi granulatio maneat, ad extremam tamen nervi pudicæ partem ubi terminatur sensus supersunt, et exquisitissima sensus gratificatio.*

If light, pressure, galvanism, or electricity produce vision, we must conclude that the idea in the mind is the result of an action excited in the eye or in the brain, not of any thing received, though caused by an impression from without. The operations of the mind are confined not by the limited nature of things created, but by the limited number of our organs of sense. By induction we know that things exist which yet are not brought

under the operation of the senses. When we have never known the operation of one of the organs of the five senses, we can never know the ideas pertaining to that sense; and what would be the effect on our minds, even constituted as they now are, with a superadded organ of sense, no man can distinctly imagine.

As we are parts of the creation, so God has bound us to the material world by this law of our nature, that it shall require excitement from without, and an operation produced by the action of things external to rouse our faculties: But that once brought into activity, the organs can be put in exercise by the mind, and be made to minister to the memory and imagination, and all the faculties of the soul.

I shall hereafter shew, that the operations of the mind are seated in the great mass of the cerebrum, while the parts of the brain to which the nerves of sense tend, strictly form the seat of the sensation, being the internal organs of sense. These organs are operated upon in two directions. They receive the impression from without, as from the eye and ear: and as their action influences the operations of the brain producing perception, so are they brought into action and suffer changes similar to that which they experience from external pressure by the operation of the will; or, as I am now treating of the subject anatomically by the operation of the great mass of the brain upon them.

In all regulated actions of the muscles we must acknowledge that they are influenced through the same nerves, by the same operation of the sensorium. Now the operations of the body are as nice and curious, and as perfectly regulated before Reason has sway, as they are at any time after, when the muscular frame might be supposed to be under the guidance of sense and reason. Instinctive motions are the operations of the same organs, the brain and nerves and muscles, which minister to reason and volition in our mature years. When the young of any animal turns to the nipple, directed by the sense of smelling, the same operations are performed, and through the same means, as afterwards when we make an effort to avoid what is noxious, or desire and move towards what is agreeable.

The operations of the brain may be said to be three-fold:

1. The frame of the body is endowed with the characters of life, and the vital parts held together as one system through the operation of the brain and nerves; and the secret operations of the vital organs suffer the controul of the brain, though we are unconscious of the thousand delicate operations which are every instant going on in the body. 2. In the second place, the instinctive motions which precede the developement of the intellectual faculties are performed through the brain and nerves. 3. In the last place, the operation of the senses in rousing the faculties of the mind, and the exercise of the mind over the moving parts of the body, is through the brain and nerves. The first of these is perfect in nature, and independent of the mind. The second is a prescribed and limited operation of the instrument of thought and agency. The last begins by imperceptible degrees, and has no limit in extent and variety. It is that to which all the rest is subservient, the end being the calling into activity and the sustaining of an intellectual being.

Thus we see that in as far as is necessary to the great system, the operation of the brain, nerves, and muscles are perfect from the beginning; and we are naturally moved to ask, Might not the operations of the mind have been thus perfect and spontaneous from the beginning as well as slowly excited into action by outward impressions? Then man would have been an insulated being, not only cut off from the inanimate world around him, but from his fellows; he would have been an individual, not a part of a whole. That he may have a motive and a spring to action, and suffer pain and pleasure, and become an intelligent being, answerable for his actions,—sensation is made to result from external impression, and reason and passion to come from the experience of good and evil; first as they are in reference to his corporeal frame, and finally as they belong to the intellectual privations and enjoyments.

The brain is a mass of soft matter, in part of a white colour, and generally striated; in part of a grey or cineritious colour, having no fibrous appearance. It has grand divisions and subdivisions: and as the forms exist before the solid bone incloses



the brain; and as the distinctions of parts are equally observable in animals whose brain is surrounded with fluid, they evidently are not accidental, but are a consequence of internal structure; or in other words they have a correspondence with distinctions in the uses of the parts of the brain.

On examining the grand divisions of the brain we are forced to admit that there are four brains. For the brain is divided longitudinally by a deep fissure; and the line of distinction can even be traced where the sides are united in substance. Whatever we observe on one side has a corresponding part on the other; and an exact resemblance and symmetry is preserved in all the lateral divisions of the brain. And so, if we take the proof of anatomy, we must admit that as the nerves are double, and the organs of sense double, so is the brain double; and every sensation conveyed to the brain is conveyed to the two lateral parts; and the operations performed must be done in both lateral portions at the same moment.

I speak of the lateral divisions of the brain being distinct brains combined in function, in order the more strongly to mark the distinction betwixt the anterior and posterior grand divisions. Betwixt the lateral parts there is a strict resemblance in form and substance: each principal part is united by transverse tracts of medullary matter; and there is every provision for their acting with perfect sympathy. On the contrary, the *cerebrum*, the anterior grand division, and the *cerebellum* the posterior grand division, have slight and indirect connection. In form and division of parts, and arrangement of white and grey matter, there is no resemblance. There is here nothing of that symmetry and correspondence of parts which is so remarkable betwixt the right and left portions.

I have found evidence that the vascular system of the cerebellum may be affected independently of the vessels of the cerebrum. I have seen the whole surface of the cerebellum studded with spots of extravasated blood as small as pin heads, so as to be quite red, while no mark of disease was upon the surface of the cerebrum. The action of vessels it is needless to say is under the influence of the parts to which they go; and

in this we have a proof of a distinct state of activity in the cerebrum and cerebellum.

From these facts, were there no others, we are entitled to conclude, that in the operations excited in the brain there cannot be such sympathy or corresponding movement in the cerebrum and cerebellum as there is betwixt the lateral portions of the cerebrum; that the anterior and posterior grand divisions of the brain perform distinct offices.

In examining this subject further, we find, when we compare the relative magnitude of the cerebrum to the other parts of the brain in man and in brutes, that in the latter the cerebrum is much smaller, having nothing of the relative magnitude and importance which in man it bears to the other parts of the nervous system; signifying that the cerebrum is the seat of those qualities of mind which distinguish man. We may observe also that the posterior grand division, or *cerebellum* remains more permanent in form: while the cerebrum changes in conformity to the organs of sense, or the endowments of the different classes of animals. In the inferior animals, for example, where there are two external organs of the same sense, there is to be found two distinct corresponding portions of cerebrum, while the cerebellum corresponds with the frame of the body.

In thinking of this subject, it is natural to expect that we should be able to put the matter to proof by experiment. But how is this to be accomplished, since any experiment direct upon the brain itself must be difficult, if not impossible?—I took this view of the subject. The *medulla spinalis* has a central division, and also a distinction into anterior and posterior fasciculi, corresponding with the anterior and posterior portions of the brain. Further we can trace down the crura of the *cerebrum* into the anterior fasciculus of the spinal marrow, and the crura of the *cerebellum* into the posterior fasciculus. I thought that here I might have an opportunity of touching the *cerebellum*, as it were, through the posterior portion of the spinal marrow, and the cerebrum by the anterior portion. To this end I made experiments which, though they were not conclusive, encouraged me in the view I had taken.

I found that injury done to the anterior portion of the spinal marrow, convulsed the animal more certainly than injury done to the posterior portion; but I found it difficult to make the experiment without injuring both portions.

Next considering that the spinal nerves have a double root, and being of opinion that the properties of the nerves are derived from their connections with the parts of the brain, I thought that I had an opportunity of putting my opinion to the test of experiment, and of proving at the same time that nerves of different endowments were in the same cord, and held together by the same sheath.

On laying bare the roots of the spinal nerves, I found that I could cut across the posterior fasciculus of nerves, which took its origin from the posterior portion of the spinal marrow without convulsing the muscles of the back; but that on touching the anterior fasciculus with the point of the knife, the muscles of the back were immediately convulsed.

Such were my reasons for concluding that the cerebrum and the cerebellum were parts distinct in function, and that every nerve possessing a double function obtained that by having a double root. I now saw the meaning of the double connection of the nerves with the spinal marrow; and also the cause of that seeming intricacy in the connections of nerves throughout their course, which were not double at their origins.

The spinal nerves being double, and having their roots in the spinal marrow, of which a portion comes from the cerebrum and a portion from the cerebellum, they convey the attributes of both grand divisions of the brain to every part; and therefore the distribution of such nerves is simple, one nerve supplying its destined part. But the nerves which come directly from the brain, come from parts of the brain which vary in operation; and in order to bestow different qualities on the parts to which the nerves are distributed, two or more nerves must be united in their course or at their final destination. Hence it is that the 1st nerve must have branches of the 5th united with it: hence the *portio dura* of the 7th pervades every where the bones of the cranium to unite with the extended branches of the 5th: hence

the union of the 3d and 5th in the orbit: hence the 9th and 5th are both sent to the tongue: hence it is, in short, that no part is sufficiently supplied by one single nerve, unless that nerve be a nerve of the spinal marrow, and have a double root, a connection (however remotely) with both the cerebrum and cerebellum. Such nerves as are single in their origin from the spinal marrow will be found either to unite in their course with some other nerve, or to be such as are acknowledged to be peculiar in their operation.

The 8th nerve is from the portion of the *medulla oblongata*\* which belongs to the cerebellum: the 9th nerve comes from the portion which belongs to the cerebrum. The first is a nerve of the class called Vital nerves, controuling secretly the operation of the body; the last is the Motor nerve of the tongue, and is an instrument of volition. Now the connections formed by the 8th nerve in its course to the viscera are endless; it seems no where sufficient for the entire purpose of a nerve; for every where it is accompanied by others, and the 9th passes to the tongue, which is already profusely supplied by the 5th.

Understanding the origin of the nerves in the brain to be the source of their powers, we look upon the connections formed betwixt distant nerves, and upon the combination of nerves in their passage, with some interest; but without this the whole is an unmeaning tissue. Seeing the seeming irregularity in one subject, we say it is accident; but finding that the connections never vary, we say only that it is strange, until we come to understand the necessity of nerves being combined in order to bestow distinct qualities on the parts to which they are sent.

The *cerebellum* when compared with the *cerebrum* is simple in its form. It has no internal tubercles or masses of cineritious matter in it. The medullary matter comes down from the cineritious cortex, and forms the *crus*; and the *crus* runs into union with the same process from the cerebrum; and they together form the *medulla spinalis*, and are continued down into the spinal marrow; and these crura or processes afford double origin to the double

\* The *medulla oblongata* is only the commencement of the spinal marrow.

nerves of the spine. The nerves proceeding from the *Crus Cerebelli* go every where (in seeming union with those from the *Crus Cerebri*); they unite the body together, and controul the actions of the bodily frame; and especially govern the operation of the viscera necessary to the continuance of life.

In all animals having a nervous system, the *cerebellum* is apparent, even though there be no *cerebrum*. The cerebrum is seen in such tribes of animals as have organs of sense, and it is seen to be near the eyes, or principal organ of sense; and sometimes it is quite separate from the *cerebellum*.

The cerebrum I consider as the grand organ by which the mind is united to the body. Into it all the nerves from the external organs of the senses enter; and from it all the nerves which are agents of the will pass out.

If this be not at once obvious, it proceeds only from the circumstance that the nerves take their origin from the different parts of the brain; and while those nerves are considered as simple cords, this circumstance stands opposed to the conclusion which otherways would be drawn. A nerve having several roots, implies that it propagates its sensation to the brain generally. But when we find that the several roots are distinct in their endowments, and are in respect to office distinct nerves; then the conclusion is unavoidable, that the portions of the brain are distinct organs of different functions.

To arrive at any understanding of the internal parts of the cerebrum, we must keep in view the relation of the nerves, and must class and distinguish the nerves, and follow them into its substance. If all ideas originate in the mind from external impulse, how can we better investigate the structure of the brain than by following the nerves, which are the means of communication betwixt the brain and the outward organs of the senses?

The nerves of sense, the olfactory, the optic, the auditory, and the gustatory nerve, are traced backwards into certain tubercles or convex bodies in the base of the brain. And I may say, that the nerves of sense either form tubercles before entering the brain, or they enter into those convexities in the base of the *cerebrum*. These convexities are the constituent parts of

the cerebrum, and are in all animals necessary parts of the organs of sense: for as certainly as we discover an animal to have an external organ of sense, we find also a medullary tubercle; whilst the superiority of animals in intelligence is shewn by the greater magnitude of the hemispheres or upper part of the cerebrum.

The convex bodies which are seated in the lower part of the cerebrum, and into which the nerves of sense enter, have extensive connexion with the hemispheres on their upper part. From the medullary matter of the hemispheres, again, there pass down, converging to the crura, Striæ, which is the medullary matter taking upon it the character of a nerve; for from the Crura Cerebri, or its prolongation in the anterior Fasciculi of the spinal marrow, go off the nerves of motion.

But with these nerves of motion which are passing outward there are nerves going inwards; nerves from the surfaces of the body; nerves of touch; and nerves of peculiar sensibility, having their seat in the body or viscera. It is not improbable that the tracts of cineritious matter which we observe in the course of the medullary matter of the brain, are the seat of such peculiar sensibilities; the organs of certain powers which seem resident in the body.

As we proceed further in the investigation of the function of the brain, the discussion becomes more hypothetical. But surely physiologists have been mistaken in supposing it necessary to prove sensibility in those parts of the brain which they are to suppose the seat of the intellectual operations. We are not to expect the same phenomena to result from the cutting or tearing of the brain as from the injury to the nerves. The function of the one is to transmit sensation; the other has a higher operation. The nature of the organs of sense is different; the sensibilities of the parts of the body are very various. If the needle piercing the retina during the operation of couching gives no remarkable pain, except in touching the common coats of the eye, ought we to imagine that the seat of the higher operations of the mind should, when injured, exhibit the same effects with the irritation of a nerve? So far therefore from thinking the parts of the

brain which are insensible, to be parts inferior (as every part has its use), I should even from this be led to imagine that they had a higher office. And if there be certain parts of the brain which are insensible, and other parts which being injured shake the animal with convulsions exhibiting phenomena similar to those of a wounded nerve, it seems to follow that the latter parts which are endowed with sensibility like the nerves are similar to them in function and use; while the parts of the brain which possess no such sensibility are different in function and organization from the nerves, and have a distinct and higher operation to perform.

If in examining the apparent structure of the brain, we find a part consisting of white medullar Striæ and fasciculated like a nerve, we should conclude that as the use of a nerve is to transmit sensation, not to perform any more peculiar function, such tracts of matter are media of communication, connecting the parts of the brain; rather than the brain itself performing the more peculiar functions. On the other hand, if masses are found in the brain unlike the matter of the nerve, and which yet occupy a place guarded as an organ of importance, we may presume that such parts have a use different from that of merely conveying sensation; we may rather look upon such parts as the seat of the higher powers.

Again, if those parts of the brain which are directly connected with the nerves, and which resemble them in structure, give pain when injured, and occasion convulsion to the animal as the nerves do when they are injured; and if on the contrary such parts as are more remote from the nerves, and of a different structure, produce no such effect when injured, we may conclude, that the office of the latter parts is more allied to the intellectual operations, less to mere sensation.

I have found at different times all the internal parts of the brain diseased without loss of sense; but I have never seen disease general on the surfaces of the hemispheres without derangement or oppression of the mind during the patient's life. In the case of derangement of mind, falling into lethargy and stupidity, I have constantly found the surface of the hemispheres dry and

preternaturally firm, the membrane separating from it with unusual facility.

If I be correct in this view of the subject, then the experiments which have been made upon the brain tend to confirm the conclusions which I should be inclined to draw from strict anatomy; viz. that the cineritious and superficial parts of the brain are the seat of the intellectual functions. For it is found that the surface of the brain is totally insensible, but that the deep and medullary part being wounded the animal is convulsed and pained.

At first it is difficult to comprehend, how the part to which every sensation is referred, and by means of which we become acquainted with the various sensations, can itself be insensible; but the consideration of the wide difference of function betwixt a part destined to receive impressions, and a part which is the seat of intellect, reconciles us to the phenomenon. It would be rather strange to find, that there were no distinction exhibited in experiments on parts evidently so different in function as the organs of the senses, the nerves, and the brain. Whether there be a difference in the matter of the nervous system, or a distinction in organization, is of little importance to our enquiries, when it is proved that their essential properties are different, though their union and co-operation be necessary to the completion of their function—the developement of the faculties by impulse from external matter.

All ideas originate in the brain: the operation producing them is the remote effect of an agitation or impression on the extremities of the nerves of sense; directly they are consequences of a change or operation in the proper organ of the sense which constitutes a part of the brain, and over these organs, once brought into action by external impulse, the mind has influence. It is provided, that the extremities of the nerves of the senses shall be susceptible each of certain qualities in matter; and betwixt the impression of the outward sense, as it may be called, and the exercise of the internal organ, there is established a connection by which the ideas excited have a permanent correspondence with the qualities of bodies which surround us.



From the cineritious matter, which is chiefly external, and forming the surface of the cerebrum; and from the grand center of medullary matter of the cerebrum, what are called the *crura* descend. These are fasciculated processes of the cerebrum, from which go off the nerves of motion, the nerves governing the muscular frame. Through the nerves of sense, the *sensorium* receives impressions, but the will is expressed through the medium of the nerves of motion. The secret operations of the bodily frame, and the connections which unite the parts of the body into a system, are through the cerebellum and nerves proceeding from it.

## BELL'S NERVE

There are two nerves spoken of as Bell's nerve, the internal and external respiratory nerves. The internal or phrenic nerve had been fully described before Bell, its function studied and its importance recognized. The external or long thoracic or posterior thoracic nerve arises from the fifth, sixth and seventh cervical nerves just after they leave the intervertebral foramina. Within the middle scalenus muscle these fibers unite to form one nerve which passes along the posterior surface of the axilla, behind the brachial plexus and axillary vessels, and down the chest wall on the outer surface of the serratus magnus (anterior) muscle, each digitation of which is supplied by a branch from the nerve. The serratus magnus holds the scapula against the chest wall, drawing it forward and laterally and aids in forced inspiration. When the external respiratory nerve is paralyzed by operations in the axilla or by blows, the vertebral border and inferior angle of the scapula hang away from the thorax and the condition of winged scapula results.

Bell's description of the nerves which now bear his name was first published in an article entitled *On the Nerves; Giving an Account of Some Experiments on Their Structure and Functions, Which Lead to a New Arrangement of the System*, published in *Philosophical Transactions of the Royal Society of London*, 111: 398-424, 1821. The article contains only one drawing, that of the nerves of the face (Plate VI). The reprint of this article in *The Nervous System of the Human Body*, Washington, D. Green, 1833, p. 39, includes two additional illustrations showing the course of the nerves. This last reference, therefore, is the one chosen for reproduction here. The article briefly describes these nerves (Bell's) and concerns chiefly the respiratory nerves of the face.

**NERVOUS SYSTEM**  
**THE HUMAN BODY;**  
EMBRACING  
**THE PAPERS**  
DELIVERED  
**TO THE ROYAL SOCIETY**  
ON THE  
**SUBJECT OF THE NERVES.**

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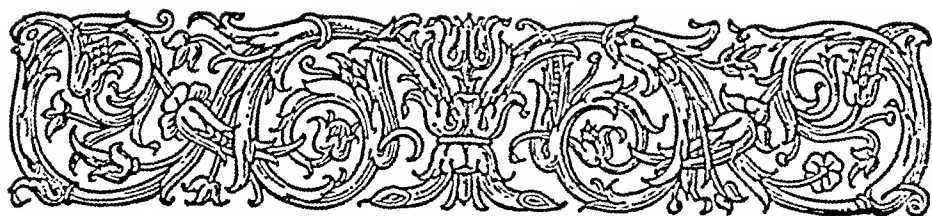
BY CHARLES BELL, F. R. S.

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1833.



## On the Nerves

Giving a View of Their Structure and Arrangement  
with the Account of Some Experiments  
Illustrative of Their Functions

BY

CHARLES BELL, F.R.S.

*[Read before the Royal Society, July 12, 1821]*

**D**URING the general advancement of science which has lately taken place in this country, observations have been gradually accumulating in the school of Windmill street, which prove that the department of anatomy has not been stationary. The nervous system, hitherto the most unsatisfactory part of the studies of the physiologist, has assumed a new character. The intricacies of that system have been unravelled, and the peculiar structure and functions of the individual nerves ascertained; so that the absolute confusion in which this subject was involved has disappeared, and the natural and simple order has been discovered.

In proceeding to give some account of these new observations, the author of this paper had conceived that it would be more suitable to the scientific body he had to address, to lay the subject before them in the precise manner in which it first presented itself to his inquiries, and to detail his observations and experiments in the succession in which they were made; but he has been persuaded by some of the members of this society to change that form, and to present the subject in the manner which he

has been accustomed to in teaching these doctrines; and they were pleased to say that, in this way, a new subject would be more readily comprehended.\*

#### INTRICACY OF THE NERVOUS SYSTEM

Anatomists have of late, not only in this country, but also in Germany and Italy, made great improvement in the minute dissection and display of the nerves; but whilst the doctrines hitherto received prevail, the discovery of new branches of nerves, and new ganglions, only involve the subject in deeper obscurity. Whilst the nerves are supposed to proceed from one great centre, to have the same structure and functions, and to be all sensible, and all of them to convey what has been vaguely called nervous power, these discoveries of new nerves and ganglions are worse than useless; they increase the intricacy, and repel inquiry. The endless confusion of the subject induces the physician, instead of taking the nervous system as the secure ground of his practice, to dismiss it from his course of study, as a subject presenting too great irregularity for legitimate investigation or reliance.

When the physiologist sees two distinct nerves spreading their branches to every part of the face, (as in the plate of these nerves,) three nerves from different sources given to the tongue, four to the throat, and nerves in most perplexing intricacy to the neck; when he finds one nerve with numerous ganglions or knots upon it, and another without them; when, in short, after a minute dissection of the nervous system, he finds a mesh, or network, spreading every where, it is not surprising that the seeming intricacy and confusion should make him, in despair, resign inquiry. But the author being forced, in the course of his duty, to go minutely over the demonstration of the nerves, year after year, without allowing himself to resign the subject merely on account of its intricacy, and finding the facts which

\* I believed that general attention to these subjects could not be raised by the account of a system founded on anatomy, and on the minute distinctions in the origins of the nerves. I thought that it required the announcement of some distinct and remarkable facts.

he had to explain in his demonstrations of the anatomy, quite inconsistent with the received opinions, he has gradually, after much study, been enabled to decypher and to read that language, of which the character had hitherto been imperfectly known. And now even the youngest students are brought to comprehend so much of the subject, that the idea of chance or accident, or real confusion among these numerous branches, is entirely dismissed; and what remains unexplained has, by the success of our past inquiries, become a subject of peculiar interest, from the conviction that attention to the minute anatomy, under the guidance of cautious and fair induction, will, sooner or later, lead to a comprehension of the whole system.

#### STATEMENT OF THE OBJECT OF THE PAPER

The author means to limit his present inquiry to *the nerves of respiration*. But, according to his conception of this matter, these nerves form a system of great extent, comprehending *all the nerves which serve to combine the muscles employed in the act of breathing and speaking*.

The first point of inquiry naturally is, how many of the muscles are combined in the act of respiration? and the second question, by what means are these muscles, which are seated apart from each other, and many of them capable of performing distinct offices, combined together in respiration? It may sound oddly to speak of the respiratory nerve of the face, of the neck, and of the shoulder; and it may be necessary to give an illustration of the sense in which the term is intended to be employed. When a post-horse has run its stage, and the circulation is hurried and the respiration excited, what is his condition? Does he breathe with his ribs only; with the muscles which raise and depress the chest? No. The flanks are in violent action; the neck as well as the chest are in powerful excitement; the nostrils as well as the throat keep time with the motion of the chest. So, if a man be excited by exercise or passion, or by whatever accelerates the pulse, the respiratory action is extended and increased; instead of the gentle and scarcely perceptible motion of the chest, as in common breathing, the shoulders are raised at each inspira-

tion, the muscles of the throat and neck are violently drawn, and the lips and nostrils move in time with the general action; if he does not breathe through the mouth, the nostrils expand, and fall in time with the rising and falling of the chest; and that apparatus of cartilages and muscles of the nose (which are as curious as the mechanism of the chest, and are for expanding these air tubes,) are as regularly in action as the levator and depressor muscles of the ribs.

It is quite obvious, that some hundred muscles thus employed in the act of breathing, or in the common actions of coughing, sneezing, speaking, and singing, cannot be associated without cords of connexion or affinity, which combine them in the performance of these actions: the nerves which serve this purpose, I call respiratory nerves.

THE NERVES OF THE ANIMAL FRAME ARE COMPLEX, IN PROPORTION TO THE VARIETY OF FUNCTIONS WHICH THE PARTS HAVE TO MAINTAIN

When we minutely and carefully examine the nerves of the human body, and compare them with those of other animals, a very singular coincidence is observed between the number of organs, the compound nature of their functions, and the number of nerves which are transmitted to them. No organ which possesses only one property or endowment has more than one nerve, however exquisite the sense or action may be; but if two nerves, coming from different sources, are directed to one part, this is a sign of a double function performed by it. If a part, or organ, have many distinct nerves, we may be certain that, instead of having a mere accumulation of nervous power, it possesses distinct powers, or enters into different combinations, in proportion to the number of its nerves. The knowledge of this circumstance gives new interest to the investigation of this part of anatomy.

Thus, in reviewing the comparative anatomy of the nerves of the mouth, we shall find, that in creatures which do not breathe, the mouth having only one function to perform, one nerve is sufficient. In certain animals, where the face and nostrils have

no complexity of relations, these parts have only a single nerve. If the throat has no complexity of organization, it has no variety of nerves. But, on the other hand, when the anatomist employs weeks to dissect and disentangle the nerves of the tongue, throat, and palate, in the human subject, he finds, at length, that he has exhibited the branches of five different trunks of nerves; and there is no clue to the labyrinth, until he considers the multiplied offices of the mouth in man; that it is a pneumatic as much as a manducatory organ; that it is the organ of the voice and of speech, as of taste and exquisite feeling. It would, indeed, be matter of surprise, if the same nerve served for the action of gnawing and feeding in the lower animals of simple structure, and also for the governance of those complicated operations, which serve to interpret the wants and sentiments of man.

Such are the views which naturally arise from an acquaintance with the nerves of the human body; but a comparison of them with those of the lower classes of animals, enables us to establish a more lucid order; and that not in an arbitrary manner, but perfectly according to nature.

THE NERVES MAY BE DIVIDED INTO TWO PARTS, OR SYSTEMS; THE ONE SIMPLE AND UNIFORM, THE OTHER IRREGULAR AND COMPLEX, IN PROPORTION TO THE COMPLEXITY OF ORGANIZATION

When the nerves of the face, mouth, throat, and neck of the human subject, are minutely displayed, it seems impracticable to reduce the numerous nerves which cross and entwine with each other, to two distinct classes; yet nothing is more certain than that this may be done, and by an easy and natural method.

The principle which is to guide us, is obtained by ascertaining what parts of the organization of an animal are necessary to life and motion; what organs are superadded as the animal advances in the scale of existence, and are necessary to higher and more complex enjoyments and actions.

Where an animal is endowed with mere sensation and locomotion, where there is no central organ of circulation, and no organ of respiration but what is generally diffused over the frame, the nerves are extremely simple; they consist of two cords running



in the length of the body, with branches going off laterally to the several divisions of the frame. And here no intricacy is to be seen, no double supply of nerves is to be observed, but each portion of the frame has an equal supply; and the central line of connexion is sufficient to combine the actions of the muscles, and to give them the concatenation necessary to locomotion.

There is the same uniform and symmetrical system of nerves in the human body as in the leech or worm; although obscured by a variety of superadded nerves. These additional nerves belong to organs which, tracing the orders of animals upwards, are observed to accumulate gradually until we arrive at the complication of the human frame. These nerves, additional and superadded to the original system, do not destroy, but only obscure that system; and, accordingly, when we separate certain nerves, the original system of simple constitution is presented even in the human body.

The nerves of the spine, the tenth or sub-occipital nerve, and the fifth or trigeminus of this system of Willis, constitute the original and symmetrical system.\* All these nerves agree in these essential circumstances: they have all double origins; they have all ganglions on one of their roots; they go out laterally to certain divisions of the body; they do not interfere to unite the divisions of the frame; they are all muscular nerves, ordering the voluntary motions of the frame; they are all exquisitely sensible; and the source of the common sensibility of the surfaces of the body: when accurately represented on paper, they are seen to pervade every part; no part is without them; and yet they are symmetrical and simple as the nerves of the lower animals.

*Comparison between the Fifth and the Spinal Nerves.*

"1. That the head and face, having many parts in every respect similar to the neck, trunk, and limbs, must have corresponding nerves.

"2. That the manner in which the spinal nerves and the fifth arise by double origins, is very similar.

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\* The following note is from a paper by Mr. Shaw. To those who have interested themselves in these discoveries, during their progress, I need not say how much I am obliged to him, and with what ability he has advocated my opinions. Often I have felt satisfied with ascertaining the facts, when he has excited me to further inquiry, and to shape them for the public.

"3. That the ganglion on the root of the fifth nerve has a strict resemblance to the ganglions at the origin of the spinal nerves.

"4. That the manner in which the branches of the fifth are distributed, and those of the spinal nerves is the same.

"And, lastly, with reference to the anatomy, we find that the same kind of connexion exists between the fifth and the sympathetic, as between the latter and the spinal nerves. In their morbid affections, the similarity also holds good: thus, in the common cases of hemiplegia, the spinal nerves and the branches of the fifth are similarly affected. In this disease, the voluntary power over the limbs, and the sensibility of the side affected, are generally destroyed; while, in some cases, the voluntary power is lost, and the sensibility continues unimpaired, or *vice versa*. This variety also occurs on the face; for the jaw will drop, and there will be all the marks of paralysis, while the sensibility of the skin and the sense of taste continue entire.

"In experiments on the nerves of the spine and on the fifth, we meet with the same results. If, as in the operation which is now frequently performed on the nerves of the horse's foot, we cut a spinal nerve after the branches are given off to the muscles moving the part, we shall destroy only the sensibility of that part; but if we cut the nerve nearer to the brain, we shall not only destroy the sensibility, but also the power of motion. The same happens in experiments on the fifth; for, if we cut a branch which is distributed principally to the skin of the lips, we shall destroy the sensibility of the part, but impair the power of mastication only in a slight degree; but if we divide the nerve further back, then we shall not only destroy the sensibility of the skin, as in the first experiment, but also cut off the power by which the jaws are moved. I cut a branch of the fifth upon the face; the sensibility of the corresponding side of the lip was destroyed, but little paralysis ensued. I cut the nerve nearer the brain, and at a point previous to its having given off the branches to the muscles; then the jaw fell, and the muscles of that side were powerless. I varied the experiment, by irritating the nerve where it lies in the pheno-palatine fissure, immediately after an animal was killed; the jaws then came together with much force, indeed, so as to nip my assistant's finger severely. This last experiment may be compared with the very common one of galvanizing the nerves which pass from the spinal marrow, to supply the muscles of the extremities."

If the nerves be exposed in a living animal, those of this class exhibit the highest degree of sensibility; while, on the contrary, nerves not of this original class or system are comparatively so little sensible, as to be immediately distinguished; in so much that the quiescence of the animal suggests a doubt whether they be sensible in any degree whatever. If the *fifth nerve*, and the *portio dura of the seventh*, be both exposed on the face of a living animal, there will not remain the slightest doubt in the mind of the experimenter which of these nerves bestows sensibility. If the nerve of this original class be divided, the skin and common substance are deprived of sensibility; but if a nerve, not of this class, be divided, it in no measure deprives the parts of their sensibility to external impression.

## MORE PARTICULARLY OF THE RESPIRATORY NERVES

The nerves which connect the internal organs of respiration with the sensibilities of remote parts, and with the respiratory muscles, are distinguished from those of which we have been speaking, by many circumstances. They do not arise by double roots; they have no ganglions on their origins; they come off from the *medulla oblongata* and the upper part of the spinal marrow; and from this origin, they diverge to those several remote parts of the frame, which are combined in the motion of respiration. These are the nerves which give the appearance of confusion to the dissection, because they cross the others, and go to parts already plentifully supplied from the other system.

The following are the nerves to be enumerated as *respiratory nerves*, according to their functions.

1. *Par vagum*, (VIIIth pair) the eighth of Willis, the *pneumogastric nerve* of the modern French physiologists. This nerve goes off from the common origin of the respiratory nerves, the lateral part of the *medulla oblongata*: it takes its course to the larynx, the lungs, the heart, and the stomach. It associates these organs together, which are at the same time supplied with nerves from other sources. Comparative anatomy would lead us to infer that this nerve is not essential to the stomach, as it does not exist but where there are heart and lungs to associate with a muscular apparatus of respiration. That the stomach must be associated with the muscular apparatus of respiration, as well as the lungs, is obvious, from the consideration of what takes place in vomiting and hiccough, which are actions of the respiratory muscles excited by irritation of the stomach.

2. *Respiratory nerve of the face*, being that which is called *portio dura* of the seventh. This nerve, like the last, goes off from the lateral part of the *medulla oblongata*, and, escaping through the temporal bone, spreads wide to the face. All those motions of the nostril, lips, or face generally, which accord with the motions of the chest in respiration, depend solely on this nerve. By the division of this nerve, the face is deprived of its consent with the lungs, and all expression of emotion. This part of the inquiry will be found very interesting.

3. *Superior respiratory nerve of the trunk*, being that which is called *spinal accessory*. This nerve has exceedingly puzzled anatomists, from the singular course which it pursues. It arises from the superior part of the spinal marrow, in a line with the roots of the other respiratory nerves. Instead of going directly out between the vertebrae, as the regular spinal nerves do, it passes up into the skull, comes out through the skull with the par vagum, and, descending upon the neck, goes to the muscles of the shoulder. In this course it supplies muscles, which are already profusely supplied by the regular system of nerves.

This nerve controls the operations of the muscles of the neck and shoulder in their office as respiratory muscles, when, by lifting the shoulders, they take the load from the chest, and fix the farther extremities of the muscles of inspiration seated on the thorax, so as to give them greater power over the ribs. When it was cut across in an experiment, the muscles of the shoulder ceased to cooperate as respiratory muscles, but remained capable of voluntary actions.

4. *Great internal respiratory nerve*, E. The *phrenic* or *diaphragmatic*, of authors. (See plates, 2, 6, and 9.) This is the only nerve of the system which has been known as a respiratory nerve. Its origin, course, and destination, are so familiar to every one, that I shall not say anything more of it here. But there is another nerve, which has a remarkable resemblance to it, and which, from circumstances already noticed, has been entirely overlooked. This is,

5. *The external respiratory nerve*. (See plates 2 and 9.) This has a similar origin with the preceding nerve. It comes out from the cervical vertebræ, and is connected with the phrenic nerve. It runs down the neck, crosses the cervical and axillary nerves, passes through the axilla, and arrives on the outside of the ribs, to supply the serratus magnus anticus, which, it is scarcely necessary to observe, is a muscle already supplied by nerves coming out between the ribs, from the system of regular nerves.

These four last-mentioned nerves govern the muscles of the face, neck, shoulders, and chest, in the actions of excited respira-

tion, and are absolutely necessary to speech and expression. But there are other nerves of the same class, which go to the tongue, throat, and windpipe, no less essential to complete the act of respiration. These are the glosso-pharyngeal nerve, and the branches of the par vagum to the superior and inferior larynx.\*

We proceed to examine the senerves in detail; and, first,

OF THE NERVES OF THE FACE, IN WHICH IT IS SHOWN THAT THE TWO SETS OF NERVES, HITHERTO SUPPOSED TO BE SIMILAR, DIFFER IN STRUCTURE, SENSIBILITY, AND FUNCTION†

It is in the face that we have the best opportunity of observing the subservience of the nerves to the uses of the parts, and of ascertaining the truth of the preceding doctrines. The human countenance performs many functions possessed by the lower creatures: in it we have combined the organs of mastication, of breathing, of natural voice and speech, and of expression. Here also are seen signs of emotions, over which we have but a very limited or imperfect control: the face serves for the lowest animal enjoyment, and partakes of the highest and most refined emotions. Happily for our present object, the nerves, which in other parts of the frame are bound together for the convenience of distribution to remote parts, are here distinct, and run apart from each other until they meet at their extremities. They take different courses through the bones of the head, and come out upon the face, to be exposed in a manner which courts inquiry.

The nerves of the face are, first, the *trigeminus*, or the fifth of Willis, and that familiarly called the *portio dura* of the seventh, but which, in this paper, will be called *the respiratory nerve of the face*.

#### OF THE TRIGEMINUS, OR FIFTH PAIR

In all animals that have a stomach, with palpi or tentacula to embrace their food, the rudiments of this nerve may be per-

\* It will be seen that, in the further investigation of this subject, the fourth nerve was discovered to be connected with this system.—See the paper on the Nerves of the Orbit.

† This subject is illustrated by plate 6, which represents the nerves of the face.

ceived; and always in the *vermes*, that part of their nervous system is most easily discerned, which surrounds the œsophagus near the mouth. If a feeler of any kind project from the head of an animal, be it the antenna of the lobster or the trunk of an elephant, it is a branch of this nerve which supplies sensibility to the member.\* But this is only if it be a simple organ of feeling, and is not in its office connected with respiration. The trunk of the elephant is not a simple feeler; it is a tube through which it respire, and therefore it has another nerve.

From the nerve that comes off from the anterior ganglion of the leech, and which supplies its mouth, we may trace up through the gradations of animals a nerve of taste and manducation, until we arrive at the complete distribution of the fifth, or trigeminus, in man. (See plate 6, in which there are its three grand divisions to the face.) Here in the highest link, as in the lowest, the nerve is subservient to the same functions. It is the nerve of taste, and of the salivary glands; of the muscles of the jaws, and of common sensibility. This nerve comes off from the base of the brain in so peculiar a situation, that it alone, of all the nerves of the head, receives roots both from the column of sensibility and of motion. A ganglion is formed upon it near its origin, though some of its filaments pass on without entering into the ganglion. Before passing out of the skull, the nerve splits into three great divisions, which are sent to the face, jaws, and tongue. Its

\* The branches of the fifth pair enter the roots of the whiskers of the cat kind, these being feelers, and requiring branches of the sensitive nerve. The following is from a paper by Mr. Shaw:

"In the cat, and in the hare, the branches of the fifth pass not only to the muscles, but also into the whiskers; while the branches of the facial respiratory nerve go past the hairs, and enter into the muscles, moving the tip of the nostril. It is rather difficult to demonstrate the nerves going into the bulbs of the hairs in these smaller animals, but it is easily done in the phoca. A preparation illustrative of this fact was shown to me some years ago in Amsterdam, by Professor Vrolich; and in the first number of the *Journal de Physiologie Experimentale*, by M. Magendie, there is an account of "*les Nerfs qui se portent aux Moustaches du Phoque*," by M. Andral. This fact of anatomy, which has been denied by some, is farther demonstrated by the dissection of those animals which have tufts of hair or whiskers over the eye. In the American squirrel, I have traced the branches of the first division of the fifth into the bulbs of the hairs over its eyebrow."

branches go minutely into the skin, and enter into all the muscles, and they are especially profuse to the lips.\*

OF THE RESPIRATORY NERVE OF THE FACE, BEING THAT WHICH IS CALLED PORTIO DURA OF THE SEVENTH†

This nerve does not exist, except where there is a necessity for some consent of motions to be established between the face and the respiratory organs; and the reason of its circuitous and prolonged course is, that it may associate with the other nerves of respiration. In fishes, this nerve, instead of being distributed forward to the face, passes backward to the muscles of the gills. In fact, there is, properly, no *portio dura* of the seventh in fishes, the nerve resembling it being a branch of the *par vagum*. A short description of this nerve in the human body will be necessary to our inquiry.

The respiratory nerve of the face arises from the superior and lateral part of the *medulla oblongata*, close to the *nodus cerebri*, and exactly where the *crus cerebelli* joins the *medulla oblongata*. The other respiratory nerves, which form so distinguished a part of the nervous system, arise in a line with the roots of this nerve.

The nerve, passing into the internal auditory foramen, is here embraced by the *portio mollis*; but it separates from it, and is received into an appropriate canal of the temporal bone. A little farther on, and while within the temporal bone, two cords of communication are formed with the branches of the fifth nerve, or *trigeminus*. One of these is called Vidian nerve, and the other *corda tympani*. By these communications, nerves go in both directions; branches of the seventh are sent to the muscles at the back of the palate; while branches of the fifth nerve (and also of the sympathetic nerve) are brought into the interior of the ear.

By the second of these communications, the *corda tympani*, [which joins the lingual branch of the fifth, just where that

\* We refer the reader to the next paper and the explanation of the plates for the more minute anatomy of this nerve.

† *Portio dura nervi acustici*. *Sympatheticus parvus* by Winslow, *Faciale* by Vicq. d'Azyr.

nerve is passing by the side of the *levator* and *circumflexus palati*,] the branches of this respiratory nerve have access to the *velum palati* and its muscles.

The respiratory nerve of the face, emerging through the stylo-mastoid foramen, divides into many branches, and these diverging, spread to all the side of the face. Let it be recollected, however, that it is here joined by branches of the third division of the fifth nerve. The respiratory nerve having escaped from the temporal bone, divides: first, a branch is sent to the muscles of the outward ear; another is sent, under the angle of the jaw, to the muscles of the throat. The principal nerve then passes through the parotid gland, and comes upon the face. Here the branches continue to scatter, to go upwards upon the temple and downwards upon the side of the neck, forming on the neck a superficial plexus. The principal branches, however, go forward to the muscles of the forehead and eyelids; a branch called superior facial is sent to the muscles of the cheek and the side of the nose; while an inferior facial branch is given to the angle of the mouth, and the muscles which concentrate there.

In this extensive distribution, the nerve penetrates to all the muscles of the face; muscles, supplied also with the branches of the fifth pair.

The descending or inferior divisions, which go under the lower jaw, and to the superficial muscles of the throat and neck, are connected with branches of the spinal nerves, and with the respiratory nerves, as may be seen in plate 6.

The proportion of the facial respiratory nerve to the fifth, is greater in man than in any other animal. If we descend to the next link in the chain of beings (the monkey,) we shall find the proportion of it to be much diminished, and that of the fifth increased. The distribution of the nerve is more complicated in the monkey than in the dog, its intricacy being apparently in proportion to the number of the muscles of expression. From the lion, the dog, and cat, we descend to the horse, ass, and cow: in these animals there is a marked difference in the distribution of the nerve, from that of either the monkey or the dog; for, excepting a few branches, which pass to the muscles of the ex-



ternal ear, and to the eyelid, the whole of the respiratory nerve is confined to the muscles of the nostrils and side of the mouth, while in the carnivorous tribes it is spread in great profusion over the cheeks and side of the neck.

There are, however, some varieties in the classes of graminivorous animals. In the gazelle, sheep, and deer, the distribution of the nerve is still more simple than in the horse; while in the camel it is more profuse, and is, in this respect, intermediate between that of the carnivorous and the graminivorous animals. The expression of the enraged camel is sufficiently ferocious; and the manner in which he shows his tusks, when dying, is very similar to that of a carnivorous creature.

If we were barely to consider this distribution of the *portio dura* of the seventh, unbiassed by theory or opinion, we should be forced to conclude, that it is not alone sufficient to supply any one part with nervous power, for every one of its branches is joined by divisions of the fifth. The question then naturally arises, whether these nerves perform the same function? whether they furnish a double supply of the same property or endowment, as so many of our best authorities have supposed? or do they perform different offices? Having taken all the assistance that the knowledge of the human structure and comparative anatomy affords, we are prepared to decide the matter by experiment.

#### EXPERIMENTS ON THE NERVES OF THE FACE, WITH A VIEW OF ASCERTAINING THE USES OF THE PORTIO DURA

If an ass be thrown, and its nostrils confined for a few seconds, so as to make it pant and forcibly dilate the nostrils at each inspiration, and if the *portio dura* be now divided on one side of the head, the motion of the nostril of the same side will instantly cease, while the other nostril will continue to expand and contract in unison with the motions of the chest.

On the division of the nerve, the animal will give no sign of pain; or in no degree equal to what results from dividing the fifth nerve.

If an ass be tied and thrown, and the superior maxillary branch of the fifth nerve exposed, touching this nerve gives acute

pain. When it is divided, no change takes place in the motion of the nostril; the cartilages continue to expand regularly in time with the other parts which combine in the act of respiration. If the same branch of the fifth be divided on the opposite side, and the animal let loose, he will not pick up his corn: the power of elevating and projecting the lip, as in gathering food, appears lost. He will press the mouth against the ground, and at length lick the oats from the ground with his tongue. In my first experiments the loss of motion of the lips in eating was so obvious, that it was thought a useless cruelty to cut the other branches of the fifth.\*

The experiment of cutting the respiratory nerve of the face, or *portio dura*, gave so little pain, that it was several times repeated on the ass and dog, and uniformly with the same effect. The side of the face remained at rest and placid, during the highest excitement of the other parts of the respiratory organs.

When the ass, on which the respiratory nerve of the face had been cut, was killed by bleeding, an unexpected opportunity was offered of ascertaining its influence, by the negation of its powers on the side of the face where it was cut across.

When an animal becomes insensible from loss of blood, the impression at the heart extends its influence in violent convulsions over all the muscles of respiration; not only is the air drawn into the chest with sudden and powerful effort, but at the same instant the muscles of the mouth, nostrils, and eye-lids, and all the side of the face, are in a violent state of spasm. In the ass, where the respiratory nerve of the face had been cut, the most remarkable contrast was exhibited in the two sides of its face; for whilst the one side was in universal and powerful contraction, the other, where the nerve was divided, remained quite placid.

From these facts we are entitled to conclude, that the *portio dura* of the seventh is the respiratory nerve of the face; that the motions of the lips, the nostrils, and the velum palati, are governed by its influence, when the muscles of these parts are in

\* The cases in the appendix prove in a more agreeable way the fact, that when the facial branches of the fifth pair of nerves are cut, insensibility results without loss of motion.

associated action with the other organs of respiration. We cannot fail to acknowledge the necessity of this relation. These passages to the lungs are membranous tubes, moved by muscles, which serve to expand and widen them, so that the air may freely enter into the lungs. It is obvious that, to produce this expansion, these muscles must have a consent with the other muscles of respiration, and move simultaneously with them; and this is affected through the respiratory nerve of the face. It shall be proved in the sequel, that the throat, neck, shoulders, and chest, have similar nerves to this, similar in distribution and function; and that these unite all the extended apparatus of breathing and speaking.

The actions of sneezing and coughing are entirely confined to the influence of the respiratory nerves. When carbonate of ammonia was put to the nostrils of the ass whose respiratory nerve had been cut, that side of the nose and face, where the nerves were entire, was curled up with the peculiar expression of sneezing; but on the other side, where the nerve was divided, the face remained quite relaxed, although the branches of the fifth pair and the sympathetic were entire. The respiratory nerve of one side of the face of a dog being cut, the same effect was produced; the action of sneezing was entirely confined to one side of the face.

These last experiments show, that the peculiar expression in sneezing results from an effect on the respiratory nerves, and that the muscles of the face are drawn into sympathy solely by the influence of the respiratory nerve of the face. It will appear that the property of receiving impression is not actually lost by the division of this facial muscular nerve, but the corresponding expression is quite destroyed.

There is no part of the nervous system where the anatomy has been more negligently consulted in forming our physiological opinions, than in what regards the office of the sympathetic nerve. The connexions of this nerve, or rather system of nerves, being universal, it has been supposed that it was the cord through which the relations of the eye, nose, face, throat, diaphragm, &c., were established, and especially in expression; whereas the

combination is effected solely through those nerves which, from their grand or leading function, I have called the respiratory nerves. The sympathetic nerve was left entire when the respiratory *portio dura* was cut, yet no sympathy pervaded the features. The sympathetic nerve is therefore not the source of that sympathy which produces expression.

It has been presumed, that the act of smiling is peculiar to the human countenance, and that in no other creature can there arise that state of enjoyment which produces this distinguishing character of the human face, the affection of benevolence, or the enjoyment of the ridiculous. But every one must have observed how near the approach is to this expression in a dog, when he fawns on his master, and leaps and twists his body and wags his tail, while at the same time he turns out the edge of the lips as like a laugh as his organs can express. When the respiratory nerve on one side of the dog's head was cut across, there was no longer this motion of the lips, although it was still observable on the other side, where the nerve was entire.

On cutting the respiratory nerve on one side of the face of a monkey, the very peculiar activity of his features on that side ceased altogether. The timid motions of his eye-lids and eye-brows were lost, and he could not wink on that side; and his lips were drawn to the other side, like a paralytic drunkard, whenever he showed his teeth in rage. Considering these facts, the conclusion is inevitable, that the motions of the lips, nostrils, and eye-lids, and forehead, in expression, have nothing to do with the fifth pair of nerves, nor with the *nervi molles*, branches of the sympathetic nerve, which accompany the blood-vessels of the face.

In the appendix we have proofs equal to experiments, that in the human face the actions of the muscles which produce smiling and laughing are a consequence of the influence of this respiratory nerve. A man had the trunk of the respiratory nerve of the face injured by a suppuration which took place anterior to the ear, and through which the nerve passed in its course to the face. It was observed, that in smiling and laughing, his mouth was drawn in a very remarkable manner to the opposite side. The

attempt to whistle was attended with a ludicrous distortion of the lips: when he took snuff and sneezed, the side where the suppuration had affected the nerve remained placid, while the opposite side exhibited the usual distortion.

Thus it appears, that whenever the action of any of the muscles of the face is associated with the act of breathing, it is performed through the operation of this respiratory nerve, or *portio dura*. I cut a tumour from before the ear of a coachman; a branch of the nerve which goes to the angle of the mouth was divided. Some time after, he returned to thank me for ridding him of a formidable disease, but complained that he could not whistle to his horses.\*

Thus it appears that the *portio dura* of the seventh nerve is the principal muscular nerve of the face; that it supplies the muscles of the cheek, the lips, the nostrils, and the eye-lids; that is, that it is the nerve which orders all those actions which have even the remotest connexion with the act of respiration. It is possible that those relations may not be apparent at first, but in the prosecution of this subject we shall discover the reasons of those links by which the respiratory organs are combined with the actions of the features.

#### OF THE FUNCTIONS OF THE TRIGEMINUS, OR FIFTH NERVE

As soon as the proper distinctions in the functions of these facial nerves are made, facts multiply upon us. We have seen that when the fifth nerve, the nerve of mastication and sensation, was cut in an ass, the animal could no longer gather his food. It was found, that on cutting the infra-orbitary branch of the fifth nerve on the left side, and the *portio dura*, or respiratory nerve, on the right side of an ass, the sensibility to pain on the right side, where the *portio dura* of the seventh nerve was cut, remained entire, while that of the left side was completely destroyed by the division of the fifth. It was also apparent in this experiment, as in the others, that there was the most marked

\* Of this we have now abundant proofs. The only subject of surprise is that these circumstances should have been so long unobserved.

difference in the sufferings of the animal, when these nerves were cut across. The cutting of the fifth nerve gave pain in a degree corresponding with our notions of the sensibility of nerves; but in cutting the *portio dura*, it was not evident that the animal suffered pain at all.

Independently of the difference of sensibility in these nerves, there was exhibited, in all these experiments, a wide distinction in their powers of exciting the muscles. The slightest touch on the *portio dura*, or respiratory nerve, convulsed the muscles of the face, whilst the animal gave no sign of pain. By means of the branches of the fifth nerve, it was not possible to excite the muscles, if the trunk of the nerve were divided; that is to say, if the communication with the sensorium were cut off.

I divided the branch of the fifth pair, which goes to the forehead, in a man, at his urgent request, on account of the *tic douloureux*: there followed no paralysis of the muscles of the eye-brow: but in an individual where an ulcer and abscess seated anterior to the tube of the ear affected the superior branch of the respiratory nerve, the eye-brow fell low, and did not follow the other when the features were animated by discourse or emotion.\*

Facts multiply upon us daily, if our attention be kept awake by a knowledge of the anatomy of these nerves. I had a patient in whom there was loss of sensibility in the side of the face and tongue from disease of the fifth, while the motions of the features remained. The case is detailed in the appendix, No. LVI. and in the next paper.

Thus experiments and occurrences in practice leave no doubt as to the distinct offices of the two nerves of the face; and that the fifth nerve is the sole cause or source of the common sensibility of the head and face.

The following circumstance occurred to a very learned and ingenious gentleman. Suffering under the pangs of toothache, he took the sudden resolution of having his tooth drawn, and by an inexperienced hand: a grinder of the lower jaw was extracted. On putting a tumbler of water to his lips, he said, Why have you

\* This is more particularly illustrated by the division of the fifth nerve.

given me a broken glass? he found presently that the glass was entire, but that he had lost the sensation of one half of his lower lip. He thought that he put half a glass to his lips, because the lip had been deprived of sensation in one half of its extent. He retained the power of moving the lip, but not of feeling in it: and now, after some years, he does not know when a portion of food, or a drop, hangs on that side of the lip, although there be not the slightest impediment in its motions.

This circumstance is explained on reference to the plate, for there is a branch of the fifth nerve called *mandibulo-labralis*, coming through the jaw, to be given to the lip. This nerve was undoubtedly hurt where it takes its course in the jaw under the roots of the teeth, and the consequence was the loss of sensation in the one half of the lip which is supplied by it. It is equally important in this investigation to notice, that, although the sensibility of the lip was destroyed by the injury of a branch of the fifth, the motion of the lip remained entire through the operation of the *portio dura*.

In the above statement there are some facts regarding the feeding of the animals which are of difficult explanation, until we consider what is necessary to the simple act of feeding. When a horse gathers the oats from the hand or from the ground, he must feel the food, which is the office of the branches of the fifth; he must move his lips under the direction of that feeling, or he cannot gather it. It was accordingly discovered by experiment, that whether the seventh or the fifth were cut, if the operation were done on both sides of the face, the creature was deprived of the power of feeding, but from different causes; for in the first experiment it was owing to the loss of motion, and in the second to the loss of sensation.

I am unable to decide whether or not the muscular branches of the fifth nerve go exclusively to the muscles of the jaws, and not at all to those of the cheeks. I have found in an individual, that, when the cheeks and lips were twisted by paralysis, he possessed the power of holding with his lips in a manner that indicated a power independent of the seventh. Now this might be a defect of one of the endowments of the seventh, whilst

another remained, or it might have been owing to a branch of the fifth going forward to the buccinator. We shall not discuss this here, as it is the subject of the second paper.\*

It will be asked, why a nerve called *respiratory* should go to the ear and the eye? First, let us inquire, does it belong to the frame of animal bodies that there shall be in them indications of passion? If it be admitted that this is the case, we here learn, in addition, that as the *portio dura* is the nerve of respiration, so is it the grand nerve of expression, not only in man, but in brutes also. All that excitement seen in a dog's head, in his eyes and ears when fighting, disappears if this nerve be cut. The respiratory nerve being cut across in a terrier, the side of the face was deprived of all expression, whether he was made to crouch, or to face an opponent and snarl. When another dog was brought near, and he began to snarl and expose his teeth, the face, which was balanced before, became twisted to one side; to that side where the nerve was entire; and the eyelids being, in this state of excitement, very differently affected, presented a sinister and ludicrous expression.

On cutting the respiratory nerve of the face in the carnivorous animals, it did not appear that the action of feeding was left so entire as in the graminivorous animals. This gave me reason to reflect on the different natures of the two classes. The beast of prey procures his food under the influence of a blood-thirsty appetite, and suffers a universal excitement; he holds and rends

\* Mr. Shaw, in a paper on this subject, says, "In the case of a little girl, the consequence of disease of the right *portio dura* is very striking. When she laughs heartily, the right cheek and the same side of the mouth are unmoved, while the muscles of the left side are convulsed with laughter.

"If told to laugh with the right side, she raises the angle of the mouth, but by an action which is evidently regulated by the fifth pair. This attempt to laugh gives a peculiarly droll expression to her face." But before we decide on this matter, we must determine whether even the *portio dura* of the seventh nerve may not lose one faculty and retain another. I suspect that the influence of passion, as this of smiling or laughing, is lost in consequence of affections that do not destroy the entire power of the nerve.

"I have observed in one patient the motions of the eyelids lost, while those of the cheek remain; in another the motions of the cheek lost, while those of the eyelids were entire. These symptoms still tend to show that one function of the *portio dura* may be lost without the other."



his prey; and especially in the larger animals of this class, the action of feeding is accompanied with horrific sounds of enjoyment; in short, with a highly excited state of the organs of respiration. In the graminivorous animals, the act of feeding is a simple and unimpassioned exercise of the organs of mastication.

The author hopes that these experiments will be deemed conclusive; yet it is a pleasanter mode of investigation to have recourse to comparative anatomy. There is only one additional instance of this kind that he will offer. It has been already stated that when a feeler, or antenna, is examined, if it be simply for sensation, one nerve only runs along it. It was suggested to him, that if this theory were true, the trunk of the elephant, being hollow, and connected with respiration, it should have two nerves; whereas, in the observations of Cuvier, it was stated to have only one; but, on examination, it was found that large branches, nearly equal in size, of the *portio dura* and of the fifth took their course along the trunk.\*

\* Mr. Shaw had an opportunity of dissecting the trunk of an elephant. He says, "from the great power which the elephant has over its trunk, I was certain that there must be large nerves running to it, similar to those which supply the fingers in man; but as the proboscis forms an important part of the respiratory system of this animal, I thought in the dissection of it there would be the most distinct proof of the accuracy or fallacy of Mr. Bell's opinions on the subject of the *portio dura*."

"The trunk was found to be supplied not only by branches of the fifth pair, as described by Cuvier, but also by a very large branch from the *portio dura* of the seventh pair."

"The *portio dura* in this elephant was found emerging from the parotid gland, as in other mammalia. It gave off some descending branches to the neck, but passed from behind the jaw to the proboscis, almost as an entire nerve, and of the size of the sciatic nerve in man: in its course it only gave some small branches to the muscles of the eye, to those of the ear, and to a small muscle which corresponds with the platysma. Before it passed into the substance of the proboscis, it united with the second division of the fifth pair, which comes forward from the infra-orbital hole, in two large branches. The two nerves being then closely united, passed between the layers of the muscles, which form the greater mass of the trunk. The *portio dura* became quickly diminished in size, as it gave off its branches in great profusion to the muscles: but the fifth was continued down, as a very large nerve, to nearly the extremity of the trunk; in this respect resembling the nerves to the fingers in man. On making sections of the proboscis, near its extremity, a great number of these nerves were seen in its substance."

"A few branches of the *portio dura* ran to the valvular apparatus in the upper part of the trunk; but this peculiar structure was supplied principally by a branch from the fifth pair, which winded round under the orbit."

SOME FURTHER REMARKS ON THE DISEASES OF  
THE NERVES OF THE FACE

Were we to inquire no further, and to rest contented with the inference, that the two sets of nerves distributed to the face have distinct functions; even this must prove useful both to the surgeon and physician. To the surgeon it must be useful in performing operations on the face, as well as in observing the symptoms of disease. If we have to plan an incision on the face, we must take especial care to avoid cutting the branches of the seventh nerve, for if it be divided, there will be paralysis of the muscles supplied by that nerve. Whereas, if we divide the fifth nerve, though there may be more pain during the operation, and a defect of sensibility following it, no unseemly distortion will be produced. To produce paralysis as a consequence of an operation which was meant to remove deformity, is an unfortunate mistake; but even worse consequences may result from an ignorance of the distinct nature of these nerves; if, trusting to the eyelids being supplied by the branches of the fifth nerve, a surgeon, in opening an abscess or cutting out a tumor, should cut the division of the seventh which goes to the eyelids, the consequence would be very unfortunate. The eyelids thenceforward would stand apart, the eye would be permanently uncovered, and the cornea become opaque, and the vision of the eye be lost.

By a knowledge of the distinct functions of the nerves of the face, combined with a knowledge of their roots or origins in the brain, we become better able to comprehend symptoms when they are consequent on disease in the bones, or in the base of the brain, or result from injury to the skull or brain, as in the case of gun-shot wounds.

To the physician the facts ascertained in this paper must also be important: he will be better able to distinguish between that paralysis which proceeds from the brain, and that partial affection of the muscles of the face, when, from a less alarming cause, they have lost the controlling influence of the respiratory nerve. How often have I seen an inflamed gland, affecting a branch of

the *portio dura*, mistaken for a disease in the brain itself, because it was not known that, although the fifth nerve was free, the pressure on the seventh nerve was sufficient to paralyse the muscles of the side of the face. That the disease of the bone at one time affects the fifth nerve, producing excessive pain of the face without paralysis; and that it, at another time, affects the seventh nerve, inducing paralysis without pain, are now phenomena accounted for.

It is very frequent for young people to have what is vulgarly called a blight; by which is meant, a slight palsy of the muscles on one side of the face, and which the physician knows is not formidable. Inflammation of glands seated behind the angle of the jaw will sometimes produce this: before these observations, it would have been said, that paralysis could not be so produced, because the parts are plentifully supplied by the branches of the fifth nerve. The occurrence is stated in the appendix. All such affections of the respiratory nerve will now be more easily detected, even in their most equivocal state: the patient has a command over the muscles of the face, he can close the lips, and the features are duly balanced; but the slightest smile is immediately attended with distortion, and in laughing and crying the paralysis becomes quite distinct.

The fact appears to be, that the respiratory motions of the face, produced by the influence of this nerve, are subject to derangement from slight causes; by causes which do not influence the general nervous system, nor even the other functions of the seventh nerve. We shall see in the third paper, that this character belongs to other branches of the same system in their distribution to the trunk.

The knowledge of the sources of expression teaches us to be more minute observers. The author had lately to watch the breathing of an infant which had been several times restored from a state of insensibility. At length the general powers fell low, without any returning fit; insensibility and loss of motion stole over the frame; all but the actions excited by the respiratory nerves ceased; then each act of respiration was attended with a twitching of the muscles of the *ala nasi*, and of that muscle of the

cheek which makes the dimple in smiling. It was then evident that the child could not recover, that all but the system of respiratory nerves had lost their powers, and the consideration that these are the last to die, showed too plainly that actual death approached.

There are conditions of the lungs, when the patient is in great danger, and yet the inflammation is not marked by the usual signs of pain and difficult motion of the chest. We shall see nothing but the twitching of those muscles of the face, which are animated by the respiratory nerve. We see a certain unusual dilatation of the nostrils, and a constrained motion of the lips, which, with the change of voice, is just sufficient to give alarm, and indicate the patient's condition. This is a state of the lungs very often produced after severe accidents as gun-shot wounds, and after great surgical operations.

A patient being in extreme danger, however debilitated, we leave him in the conviction that death does not yet approach; but when the respiratory organs are agitated, then the act of dying has commenced.

These circumstances are stated to prove that the subject of expression is not foreign to medical studies; and certainly, by attention to the action of the muscles of the face, we shall find the views drawn here from the anatomy farther countenanced. We learn that smiling is an affection of the nerve of respiration on the muscles of the face, and that when laughter shakes the sides, it is only an extended and more convulsive action of the muscles, produced by the same class of nerves. When to the paleness and coldness and inanimation of grief, there is added the convulsive sob and the catching of the throat, and the twitching of the lips and nostrils, we discover the same class of nerves to be affected, which, in crying, are only more obviously in operation, producing more violent contractions.

## CONCLUSION

When the account of the nerves of the throat, neck, and chest, shall be laid before the society, as those of the face have now

been, and when a comparison shall be made of the varieties in nerves corresponding with the changes in the mechanism of respiration in different animals, a juster estimate may be formed of the importance of these observations. Then the same distinctions of structure and function, which are made manifest in the nerves of the face, will be observed in nerves which take an extensive course through the body. We shall be able to distinguish and separate the nerves of respiration, amidst the apparent intricacy of the general system. By cutting across these nerves of respiration, we shall find it possible successively to stop the motions of the several parts which unite in the act of respiration; not only to stop the motion of the diaphragm, but the motions of the side, of the shoulder, of the larynx or the pharynx, by cutting their respective respiratory nerves. When this is done, they will be left in the exercise of their other functions through their other nerves, and still alive to other excitements, and capable of performing the voluntary motions, though dead to the influence of the heart and lungs.

By thus distinguishing the nerves of respiration, and as it were separating them from the others, we reduce the remaining part of the nervous system to comparative simplicity. The seeming intricacy in the branching of the nerves, their convergence to certain organs from different origins, their re-union and divergence, instead of being a source of confusion, become a subject of the highest interest. The re-union and crossing of nerves we now ascertain to be for the purpose of associating the muscles into different classes, for combining them in subserviency to different organs, and placing them under the guidance of a sensibility more certain in its operation than the will.

And now it may be once more asked, why is the *portio dura*, the muscular nerve of the face, separated from the sensitive fifth pair? Is it an accidental circumstance? No, certainly: it is a dangerous principle to admit chance in a matter of this kind: it cannot be an accident, which directs a distribution so uniform through all the varieties of animals which breathe. It is ordered for the ends so often hinted at in these papers—that the organs in the face may be associated with those of the neck, larynx,

pharynx, &c. The nerve separates from the fifth, and joins the glosso-pharyngeal and laryngeal, and the roots of the phrenic, that all the parts supplied by these may be joined together, and that a sympathy may exist among those parts which would remain disjoined were there no other nerves than the regular and symmetrical nerves of the spinal marrow.

## A VIEW OF THE NERVES OF THE HEAD

### EXPLANATION OF PLATE VI

In this plate the two distinct classes of nerve which go to the face are represented; the one to bestow sensibility, and the other motion, and particularly the motions of speaking and expression, that is, the actions connected with the respiratory organs.

The nerves on the side of the neck are also represented. These I have discovered to be double nerves, performing two functions: they control the muscular frame, and bestow sensibility on the skin. Besides these regular spinal nerves, which are for the common endowments, the nerves of the throat are represented. These latter nerves are the chords of sympathy which connect the motions of the neck and throat with the motions of the nostrils and lips; not merely in swallowing and during excited respiration, but in the expression of passion, &c.

- A. The respiratory nerve of the face, or, according to authors, the *portio dura* of the seventh nerve.
  - a. Branches ascending to the temple and side of the head.
  - b. Branches which supply the eyelids.
  - c. Branches going to the muscles which move the nostrils.
  - d. Branches going down upon the side of the neck and throat.
  - e. Superficial cervical plexus.
  - f. Connexions formed with the cervical nerves.
  - g. A nerve to the muscles on the back of the ear.
- B. The eighth nerve, *par vagum*, or grand respiratory nerve.
- C. The superior respiratory nerve, or spinal accessory nerve.
- D. Ninth nerve, or *lingualis*.
- E. Diaphragmatic, or phrenic nerve.
- F. Sympathetic nerve.

- G. Laryngeal nerve.
- H. Recurrent laryngeal nerve.
- I. Glosso-pharyngeal nerve.
- I. Frontal nerve: a branch of the fifth. '
- II. Superior maxillary nerve: a branch of the fifth.
- III. Mandibulo-labialis: a branch of the fifth.
- IV. Temporal branches of the third division of the fifth.
- V. Ramus buccinalis-labialis: a branch of the third division of the fifth, prolonged from the motor root.
- VI. VII. VIII. IX. Spinal nerves.

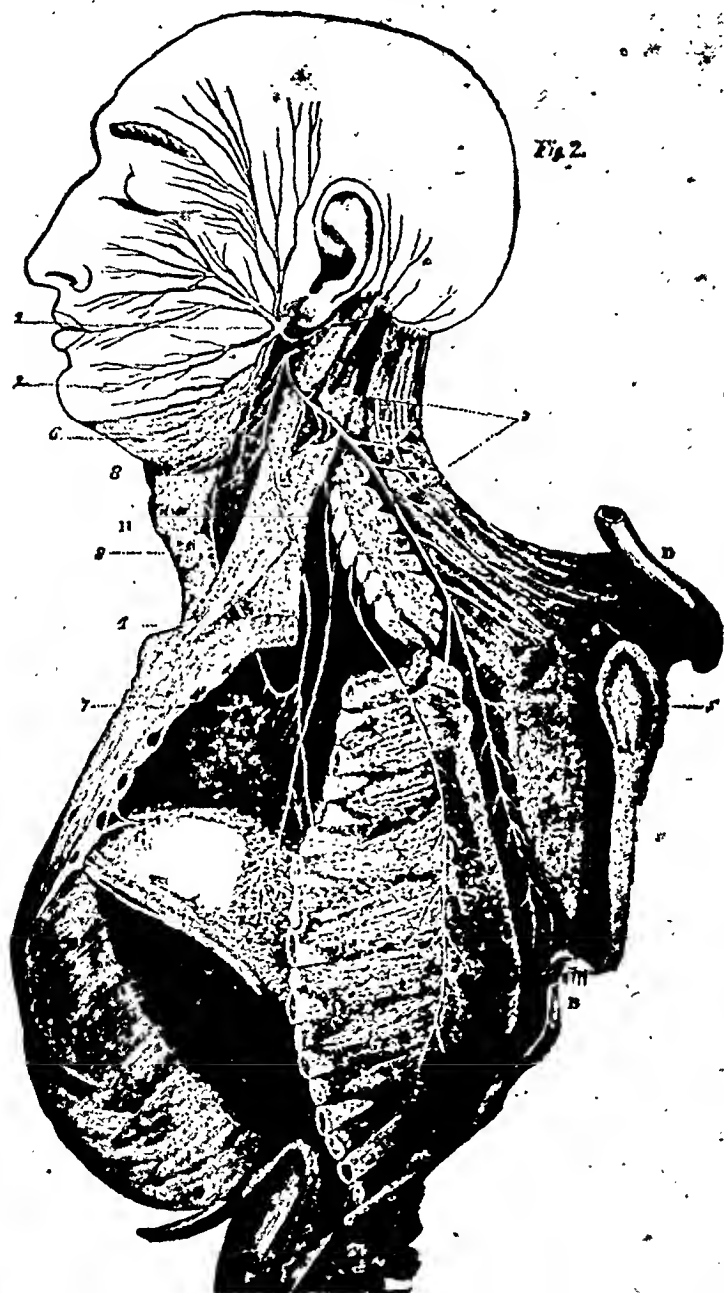
## BELL'S PALSY

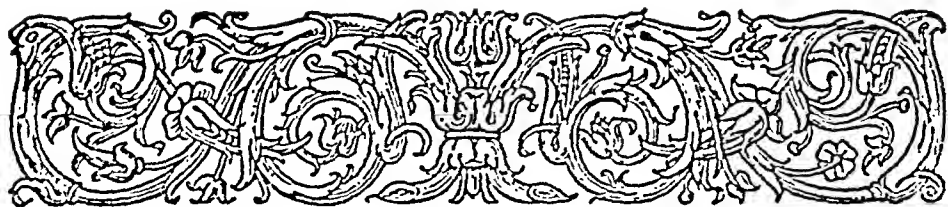
Bell's palsy is the name applied to facial paralysis due to extracranial or peripheral involvement of the seventh cranial nerve by injury, inflammation from exposure to cold, infection or pressure of a tumor—malignancy of the parotid gland. The forehead cannot be wrinkled, the eye cannot be closed on the affected side (Bell's phenomenon or sign). The naso-labial fold is smoothed out, the angle of the mouth, lower than normal, cannot be raised. Whistling is impossible and speech imperfect because the lips cannot be properly closed.

This condition was first briefly described by Charles Bell in a paper *On the nerves; giving an account of some experiments on their structure and functions, which lead to a new arrangement of the system*, published in the Philosophical Transactions of the Royal Society of London, 111: 398-424, 1821. In 1829 he presented a further report, *On the nerves of the face; being a second paper on that subject*, in which he gave a more detailed description of the condition and corrected his previous mistakes. The second paper has been chosen for reproduction in the following pages. For the first paper see Bell's nerve.



Fig. 2.





## XXVI. On the Nerves of the Face

Being a Second Paper on That Subject

BY

CHARLES BELL, ESQ.

*Fellow of the Royal Society*

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Read May 28, 1829

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**I**HAVE to beg the indulgence of the Society to some minute details of anatomy, for the sake of those deductions which can be attained by no other means: and that a zeal for its cultivation may be preserved among us. There is an obvious practical benefit derived from anatomy, but the public do not comprehend its importance as a science. It is to the Royal Society that those who prosecute this science must look for countenance in their slow and painful investigations.

Nine years ago, at the request of our late President, I submitted to the Society a paper on the Nervous System; in which I arranged the nerves strictly according to the anatomy, and illustrated the principles of the arrangement, by exhibiting the different functions of the Nerves of the Face. On presenting a second paper on the same part of the nervous system after so considerable a lapse of time, there will be some novelty both in the facts and in the illustrations; yet I have more gratification in showing that after the most minute inquiries in different coun-

tries, my positions drawn from the anatomy have been admitted, and my reasoning on the experiments, with one exception, found to be correct. Confident in the accuracy of my deductions from the anatomy of the fifth nerve, I had attributed to one of its branches a function which belongs to another branch of the same nerve. The subject will form a part of the present paper.

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After the announcement of the facts in my first paper, the inquiry became interesting from its application to medical practice. I must take another opportunity of thanking those gentlemen who have so liberally afforded additional proofs of the truth of my principles. I must restrict myself in referring to them here, since I am desirous that the Society's Transactions should contain only the philosophical part of the inquiry.

The system of WILLIS, of which we have an elegant account in the posthumous works of DR. BAILLIE, prevailed universally in the schools when I entered on these inquiries. In opposition to that system I demonstrated that the nerves hitherto supposed to possess the same powers, consisted of filaments having different roots, and performing different functions. I found myself embarked in this investigation, from observing the course which the nerves took in their distribution through the body. Conceiving that the devious course and reunion of the nerves were for a purpose, I sought in their origins for the cause of their seeming irregularity. It was discovered that the roots of the nerves arose from distinct columns of nervous matter, and that on these columns depended their different properties. Those which were called the common nerves, that is, the nerves which arise from the spinal marrow, thirty in number, were found to consist each of two nerves derived from distinct columns, one for sensation and one for motion. In the further pursuit of this subject, there was reason to conclude that the spinal marrow contained not only the columns for bestowing sensation and motion, but also another column, the office of which was to combine the actions of respiration. I then drew the attention of the Society to the course of the fifth nerve of the brain according to WILLIS. I showed that it had the same double root as the

spinal nerves, that it had a ganglion, and that part of the nerve passed free of the ganglion; and that from all these points of resemblance, it was to be considered as the anterior or superior of the spinal nerves, of that system which is called symmetrical, and which ministers to the same functions in all classes of animals, bestowing sensibility and the locomotive powers, but deficient in those filaments which command the respiratory motions. I am particular in restating this, because from time to time it has been reported that I had abandoned my original opinions; whereas every thing has tended to confirm them.

From the general view of the nervous system, I drew attention to the superadded or irregular nerves. Having shown that the original or symmetrical system of nerves, of which the fifth was one, had no power over the motions of respiration, and that the human countenance in all its motions, with the exception of mastication, bore relation to the actions of respiration, it was therefore required that another nerve besides the fifth, should be sent to the face. Having shown also that the roots of the fifth nerve were distant from that column of nervous matter which gives origin to the nerves of the respiratory system, and that it could not therefore minister to the motions of the face which are connected with respiration; and that another nerve, the portio dura, having its root in common with the nerves of respiration, took its course to the face,—the subject was prepared for experiment.

By experiments on the nerves of the face these three things were proved: First, that the sensibility of the head and face depended on the fifth pair of nerves. Secondly, that the muscular branches of the fifth were for mastication: and in the Third place, it was proved that the portio dura of the seventh, or respiratory nerve of the face, controlled the motions of the features, performing all those motions, voluntary or involuntary, which are necessarily connected with respiration;—such as breathing, sucking, swallowing, and speaking, with all the varieties of expression.

Reserving the details, I shall now state shortly the occurrences which I have witnessed since the publication of that paper;

as they afford convincing proofs of the correctness of these opinions.

The first instance was in a man shot with a pistol ball, which entered the ear and tore across the portio dura at its root. All motion on the same side of the face from that time ceased; but he continued in possession of the sensibility of the integuments of that side of the face.

The next instance was in a man wounded by the horn of an ox. The point of the horn entered under the angle of the jaw and came out before the ear, tearing across the portio dura. He remains now a singular proof of the effects of the loss of function in the muscles of the face by this nerve being divided. The forehead of the corresponding side is without motion, the eyelids remain open, the nostril has no motion in breathing, and the mouth is drawn to the opposite side. The muscles of the face by long disuse are degenerated, and the integuments of the wounded side of the face are become like a membrane stretched over the skull. They have lost their firmness, and the flesh under them is wasted, with the exception of certain muscles, the reason of which will be understood on perusing the anatomical description in the present paper. In this man the sensibility of the face is perfect. The same nerve (portio dura) has been divided in the extirpation of a tumour from before the ear, and the immediate effect has been horrible distortion of the face by the prevalence of the muscles of the opposite side, but without the loss of sensibility; and that distortion is unhappily increased when a pleasurable emotion should be reflected in the countenance.

These facts are so distinct, that I cannot presume to detain the Society with the instances of the lesser defects which I have witnessed from the more partial injuries or temporary diseases of the nerve;—such as distortion of the features produced by glands pressing on this nerve, paralysis from suppurations in the ear affecting the nerve in its passage, or temporary derangement disturbing one or more of its functions.

As to the fifth nerve, the facts are equally impressive, and correspond with our former experiments and opinions. By a

small sacculated tumour affecting the roots of this nerve, the sensibility was destroyed in all the parts supplied by its widely extended branches; that is, in all the side of the head and face and the side of the tongue, whilst the motion of the face remained. Two circumstances affecting this nerve have occurred with most curious coincidence in the symptoms. By the drawing of a tooth from the lower jaw, the nerve which comes out upon the chin to supply one half of the lip was injured, and exactly this half of the lip was rendered insensible. When the patient put his mouth to a tumbler he thought they had given him a broken glass! Precisely the same thing occurred from the division of that branch of the fifth nerve, which goes to one half of the upper lip. A gentleman falling, a sharp point entered his cheek and divided the infra orbitary nerve: the effect was loss of sensation without loss of motion, in that half of the upper lip to which the nerve is distributed. The remarkable circumstance was, that this individual made the same remark when the cup was put to his lip:—that they had given him a broken one! The part of the cup which was placed in contact with the insensible portion of the lip appeared to him to be broken off.

I have had two or three instances before me of disease affecting the ophthalmic branch of the fifth nerve, and producing total insensibility of the eye and eyelids, without loss of vision; whilst the eyelids continued to be closed and the eyebrow to be moved by the influence of the portio dura of the seventh nerve.

Such are a few of the facts which have been reaped from a patient reliance on the correctness of my first deductions, and I would now urge them in proof of the importance of reasoning upon the anatomy. All these nerves have been repeatedly divided, by almost every surgeon of eminence in the three kingdoms. Although some have performed the operation of dividing the nerves frequently, and one eminent gentleman had done it six times on the face of the same man, all these operations have been performed without giving rise to the suspicion that these nerves bestowed different properties. Even now, so slow is the progress of improvement, it is stated by a surgeon that he will not hesitate to cut the portio dura in the case of tic

douloureux. My duty is performed when I give publicity to the facts which prove that horrible distortion of the whole countenance, the loss of distinct articulation, the loss of expression, the loss of motion of the eyelids, and consequent inflammation of the eye, must follow such an operation.

Much has been said in favour of experiments when made by men who are positively without any expectation of the result, or, as they affirm, are unbiassed. The only instances of this that I can allow, are when the surgeon cuts the nerves of the face in a surgical operation. In such operations as these for tic douloureux, he is indeed unbiassed; and we have seen the result, that after fifty years of such experience we remained quite ignorant of the distinctions in these nerves. But on the other hand when attention is roused to inquiry by anatomy, facts are obtained of the utmost importance both to the knowledge of disease and to the safe practice of surgery.

#### OF THE MOTOR OR MANDUCATORY PORTION OF THE FIFTH NERVE

The fifth nerve is usually called Trigemini, from piercing the skull in three grand divisions. But when it has been shown that it is composed of two distinct roots having different functions, the accidental circumstance of its divisions passing through the bones yields in importance to another inquiry, How is the muscular portion of the nerve distributed?

Since the publication of my first paper this inquiry has assumed importance; although the principal facts of the anatomy were known to WRISBERG, SANTORINI, PALETTA, PROCHASKA, and SÆMMERRING. But in no author is the anatomy of the motor portion of the nerve traced with sufficient minuteness, or regard to the distinct uses of the muscular and sensitive divisions.

The motor division of the fifth nerve passes under the Gasserian ganglion, and free of it. It is not seen when we look from above, as in the plates of MONRO. When the nerve is turned up and dissected, this portion is seen to form about a fifth part of the whole nerve. It is tied to the larger portion before advancing to the ganglion, by filaments which have been sometimes taken for nerves.

Having passed the ganglion, it attaches itself slightly to the superior maxillary nerve, but this is apparently a membranous connection only.\* The nerve itself joins the third grand division after passing the foramen ovale. At this point the muscular and sensitive portions of the nerves are matted together, and form a mass which between the fingers feels like a knot.† There is, however, no red and fleshy-like matter interposed here, as in the Gasserian ganglion of the trunk of the nerve. But the filaments of both portions of the nerve are here so complexly and intimately combined, that all the branches which go off after this union are compound nerves, and have motor filaments in their composition.

It is, however, equally obvious that the gustatory division of the nerve which descends from this mass, has not the muscular portion given to it in that abundance which those branches have which take their course to the muscles of the jaws. The mandibulo-labralis, which also descends from this plexus, lies nearer the motor portion, and has a more distinct addition given to it than the gustatory nerve.

This motor or muscular portion which we are tracing, sends off no branch either in its course under the great ganglion, or after passing it about half an inch. But when it has arrived at the point of union with the ganglionic portion, the filaments become interwoven; and from this place the nerves are compound, and go off diverging to their destinations. First, there are sent off nerves to the temporal, masseter, and pterygoid, muscles, also to the buccinator muscle. The temporal muscle receives a large and appropriate nerve. The nerve to the masseter passes between the coronoid and condyloid processes of the lower jawbone; but before going into the muscle it sends branches to the temporal muscle. The pterygoid muscles have each their appropriate nerves coming direct from this plexus.

\* GERARDI, commenting on SANTORINI, says that the anterior root (the motor) does give filaments to the superior maxillary division of the fifth. PROCHASKA (*de Structura Nervorum*) gives two views, Tab. ii. fig. v. vi. which represent an actual union of the anterior root and the superior maxillary nerve. In the plate, however, the twigs seem rather to go from the ganglionic into the motor division.

† SANTORINI says, it is a plexus like a ganglion, "in plexum vere ganglioformem mutatur."



## RAMUS BUCCINALIS LABIALIS

This is a remarkable branch which arises from the same source, and goes to the cheek and lips. This nerve where it lies on the external pterygoid muscle sends one more branch to the temporal muscle; it then divides, one branch enters the buccinator muscle, and another is prolonged forwards. The division to the buccinator muscle is tortuous, which is no doubt a provision for its being undisturbed by the free motion of the cheek; its minute branches may be traced until lost among the muscular fibres, whilst others penetrate to the lining of the cheek. The prolonged branch is the labial division; it runs nearer the alveolar processes of the lower jaw, and becomes so superficial as to admit a union with the portio dura: from thence passing under the facial artery it may be traced into the triangularis or depressor anguli oris, the levator labiorum communis, and the lateral portion of the orbicularis oris.

In the distribution of the buccinalis labialis to the muscles of the mouth, it is joined, as I have said, by branches of the portio dura; and nothing is more striking than the manner in which this latter nerve passes over the masseter, a muscle of the jaw, to be profusely given to the muscles of the lips.

There is one more branch important to the physiology of the fifth nerve. At the root of the mandibulo-labralis (where it is sent off from the junction of the muscular and ganglionic portions), a small nerve takes its origin. This branch runs parallel to the greater nerve till it enters the foramen in the lower jaw; here it seems to enter, but does not; it takes a course on the inside of the jaw to arrive at its final destination, the mylo-hyoideus and the anterior belly of the digastricus, that is, to those muscles which open the mouth by drawing down the jaw.

We may for a moment interrupt our particular inquiry, to notice that all muscular nerves, and consequently the muscular divisions of the fifth nerve, form a plexus. The plexus, formed by the motor and ganglionic divisions of the fifth nerve before they diverge to the muscles of the lower jaw, corresponds with the plexus formed on the nerves sent to other classes of muscles. Even that branch of the third division of the fifth nerve which

comes out before the ear, joins the portio dura in a plexus;\* and this is the reason of that sensibility evinced in the facial nerve in making experiments upon it.

The form of the fifth nerve, and its resemblance to the spinal nerves, had struck some of the best continental anatomists. But as they had made no distinctions in the functions of the roots of the spinal nerves, so neither did they imagine any difference in the roots of the fifth nerve, and therefore no consequence resulted from having observed this resemblance. This part of the anatomy, together with the whole minute relations of the nerves, was a dead letter, and led to no inference.

But now resuming the course I have hitherto followed, the anatomy of the fifth nerve points to curious results. We see that the motor division of this nerve goes first to the muscles which close the jaw and give it the lateral or grinding motions. Secondly, we see that it is distributed to the muscles of the cheek, which place the morsel under the operation of the teeth; and thirdly, we find it going to the muscles which open the jaws.

We proceed to the second method of proof, by experiment. Does the fifth nerve move the jaw? is it indeed the manducatory nerve as suggested by the anatomy? Let the following experiments determine the fact.

#### EXPERIMENT I

The root of the fifth nerve being exposed in an ass and irritated, the jaws closed with a snap.

#### EXPERIMENT II

The fifth pair being divided in an ass, the jaw fell relaxed and powerless.

If we consider the action of mastication, we shall see what the consequence would be, were there no accordance between the motions of the lower jaw and the cheeks. Conceiving that there must be such an accordance, and contemplating the roots of the

\* See the adjoined plate.

fifth pair and their distinct functions, I had imagined that this office was performed by the branches of the second division of the fifth. But finding that the connection between the motor root and the superior maxillary nerve proved to be only by cellular texture, and considering the affirmation of M. MAGENDIE and those who followed him, that the infra-orbitary branch had no influence upon the lips, I prosecuted with more interest the *Ramus Buccinalis Labialis*. And nobody, I presume, will doubt that the distribution of this division confirms the notions drawn from the anatomy of the trunk,—not only that the fifth nerve is the manducatory nerve as belongs to the muscles of the jaws, but also that it is distributed to the muscles of the cheek and lips to bring them into correspondence with the motions of the jaws. Let us take in illustration the articulation of the bones. In the joints the muscles are attached to the capsular membrane in such a manner as to draw it from between the bones and adapt it to the degree of flexion of the joint. If the cheek were a passive membrane like the capsule of a joint, it would have required some such mechanical connection with the jaw or its muscles, as might have drawn it from between the teeth in the motions of mastication. But being a muscular part, to bring it into just relation with the motions of the teeth, it must have an accordance through nerves, and act in sympathy;—relax when the jaws are apart, and contract when they are closed. I think therefore we may perceive why a branch of the motor nerve of the muscles of the jaws sends a division to the muscles of the cheek and to the angle of the mouth.

By such a process of reasoning we see also why a branch of the same nerve should prolong its course under the chin to the muscles which are opponents to those which close the jaw.

In short, the motor portion of the fifth nerve sends no twigs with the ophthalmic division, nor the superior maxillary nerve, but only with the lower maxillary nerve. To the muscles of the lower jaw alone which are in action during mastication, and to the muscles necessarily associated in that action, the manducatory nerve is distributed.

It remains only that we observe what takes place in man, and compare the circumstances with experiments on brutes.

I was consulted in the case of a lady with an uncommon disease in the side of the head: the description of her condition puzzled me very much; there was so much said of tumours with pulsation on the head and face. But when I saw and examined her, the mystery disappeared; she had powerful spasms of the temporal and masseter muscles, which rose and swelled, under the excitement of a disease of the cheek, and with a pressure of the jaws so powerful as to displace the teeth. During this violent spasm of the muscles supplied by the fifth nerve, the motions of the features were free and unconstrained under the influence of the portio dura of the seventh nerve.

I have the precise counter-part to this morbid condition of the muscles of mastication in the case of a poor man now under my care. He has a disease affecting the fifth nerve of the left side, attended with the loss of sensibility of the side of the face and of the surfaces of the eye. In him there is no motion of the muscles of the jaw of the affected side. In chewing, the action is only on the right side of the head; the masseter muscle and temporal muscle of the left side do not rise or bulge out as in their natural actions; but his command over his features is perfect through the operation of the portio dura. It appears, therefore, that the disease of the fifth nerve, which has destroyed the sensibility on one side of the face, has caused a loss of motion in the muscles of the jaw on the same side.

A more frequent occurrence establishing the distinction of motions influenced by the fifth and seventh nerves, is presented in the case of paralysis of the portio dura; for then all the muscles waste but those supplied by the fifth. In the case referred to, of the man wounded by the horn of an ox, in whom the portio dura was torn, and who had the skin of his forehead, side of the nose, cheek and lips, deprived of all fleshiness and substance, and in fact wasted to mere skin, the muscles of the jaw were entire and prominent; and on introducing the finger into the mouth and making him imitate the motions of mastication, a weak contraction could be felt in the cheek.\*

These facts close the evidence of the fifth nerve being a double

\* How often a question has occurred as to this motion in the cheeks, may be seen on referring to cases, p. 123, Exposition, &c. and p. 57, Appendix, 1st edition.

nerve; not only the nerve of sensibility to the head and face, but a muscular nerve to the muscles of the jaws, active in mastication, and otherwise useful in all animals whose jaws are prehensile and used as hands. This curious fact, originally drawn from the anatomy and now confirmed by it, had nearly been obscured by experiment; since the external branches of the fifth nerve, those most exposed to the experimenter, are not muscular.

I am bound to acknowledge here the correction by M. MAGENDIE, in regard to the office of the suborbital division of this nerve, since it has given occasion to the revisal of the anatomy.\*

We were involved in great confusion by the discovery of new branches of nerves and of ganglions, through which we had no guide, until we formed a correct arrangement of the whole system. It is satisfactory to find that the ideas first suggested by a comparison between the roots of the nerves and their complex distribution in the face and neck are correct, when tried by a minute investigation of the internal nerves of the head; and that the conclusions drawn from the anatomy, are confirmed both by experiment and by a knowledge of the effects of injuries and of disease in the human frame.

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ADDITIONAL NOTE.—As the most important fact in this paper is that ascertained by experiments on the fifth nerve, I am bound to say by whom they were made, and for what purpose.

To my late brother-in-law Mr. JOHN SHAW, whom I educated, I have been indebted through the whole of this inquiry. He had long been acquainted in the most intimate manner with my pursuits. He had repeated my experiments on the roots of the spinal nerves, confirming the results,—that the anterior roots when irritated caused the muscles to contract, and that the posterior roots had no such influence.

He assisted me in my experiments on the nerves of the face, which were for the purpose of establishing that the fifth pair

\* M. MAGENDIE says, "Le résultat que nous avons obtenu s'accorde parfaitement avec celui que nous venons de rapporter, à l'exception toutefois de l'influence de la section de sous-orbitaire sur la mastication, influence qui n'a pas été évidente pour moi."—*Journal de Physiologie*, 1821.

resembled the nerves of the spine, and at the same time proving, what was incomplete from the experiments on the spinal nerves, that a ganglion on one of the roots of a nerve is no cause of interruption to sensation, but the sign that it bestows sensibility; making certain what could be only assumed from the experiments on the spinal nerves.

But he was acquainted also with my opinions drawn from the distribution of the nerves in the body contrasted with the anatomy of their roots. And when the correctness of these opinions was established by experiment, he let no opportunity pass of advocating and supporting them. In collecting information and making dissections he was ever active, as all the real students educated with him will testify. It was in the fervour of his zeal that he went to Paris and explained the arrangement by which I distinguished the nerves, and repeated my experiments with M. MAGENDIE and others at Charenton near Paris in 1821.

At this time an idea was thrown out that the fifth nerve was no more than the sensitive nerve of the face accidentally separated from the muscular nerve (the portio dura). Perceiving that if this notion prevailed we should be thrown back into our former state of confusion, and to put the matter beyond all question, Mr. SHAW performed those experiments which are contained in this paper,—experiments which in the gentleness of his nature he would have hesitated to make from their severity, but for their being imperatively called for.

Had Mr. SHAW lived, this subject would have been further advanced. Whilst his excellent judgement and indefatigable exertions aided me in every difficulty, his gratification in witnessing the progress of these inquiries was a reward beyond what I have now to look for.

#### EXPLANATION OF PLATE VIII

In this figure the superficial nerves of the face are turned off, and the distribution of the third division of the fifth to the muscles of the jaws and cheek exposed.

A. The portio dura of the seventh or respiratory nerve of the

face coming out from the stylomastoid foramen; the principal branches are cut and folded forwards.

B. The trunk of the portio dura of the seventh, dissected off the face and pinned out, while it is left at its connections with the branches of the fifth on the cheek and lips.

C. The branch of the third division of the fifth nerve, which joins the plexus of the portio dura before the ear. Some experimenters, ignorant of this junction of a sensitive nerve with the muscular nerve, have occupied themselves with experiments to ascertain the degree of sensibility of the portio dura.

D. In this figure the masseter muscle is dissected from the jaw-bone and lifted up to show D, the branch of the fifth pair of nerves going into the muscle.

E. The Ramus Buccinalis-labialis, the branch of the fifth nerve which goes to the buccinator, triangularis, levator labiorum, and orbicularis muscles.

F. That branch of the fifth nerve which separating from the mandibulo-labralis goes to the muscles which depress the lower jaw.

G. The suborbital nerve, a branch of the fifth nerve.

H. The mandibulo-labralis, a branch of the fifth nerve coming out from the bone to the muscles and integuments of the lip and chin.

I. A branch of the fifth nerve descending from the orbit.

D, E, F, are muscular branches of the fifth nerve, and are motor nerves. C, G, H, I, are sensitive branches of the same nerve which join the branches of the portio dura in its universal distribution; and although these branches of the fifth enter the muscles, they possess no power over their motions. B is the portio dura, which, though taking the same course with the last, is for a different purpose; while it is a motor nerve, by its association with the respiratory nerves, it is enabled to excite those actions of the face and lips which are necessarily connected with the act of breathing.

#### EXPLANATION OF PLATE IX

Fig. 1. Represents the fifth nerve dissected out and seen on its lower surface.

- A. The posterior sensitive root before it forms the ganglion.
- B. The Gasserian ganglion.
- C. The anterior or motor root of the nerve passing the ganglion.
- D. The third or lower maxillary division of the fifth nerve.
- E. The motor portion joining the lower maxillary nerve and forming a plexus with it. From this plexus go off the muscular nerves to the muscles of the jaw, viz.
  - 1. Temporalis.
  - 2. Massetericus.
  - 3. Buccinalis labialis.
  - 4. Pterygoideus.
  - 5. Mylo-hyoideus.
- F. Division which joins the portio dura.
- G. Mandibulo-labralis.
- H. Gustatory nerve.
- I. The chorda tympani.

Fig. 2. This figure represents the ganglion on one of the spinal nerves, to show its resemblance to the ganglion of the fifth nerve in every particular.

- A. The posterior or sensitive root of the nerve.
- B. The ganglion formed upon the posterior root.
- C. The anterior or motor root of the nerve; this arises in minute branches which join to form the larger subdivisions, whilst the posterior root is composed of simple and abrupt portions. This division joins the sensitive division beyond the ganglion exactly in the same manner that the motor portion of the fifth joins the lower maxillary nerve.

Fig. 3. Represents one of the ganglions of the sympathetic nerve to show how different it is from those on the symmetrical system of nerves. In fig. 1 and 2 the nerve on entering the ganglion and escaping from it, is separated into branches in a manner very different from the mode in which the sympathetic nerve joins or forms its ganglions.\*

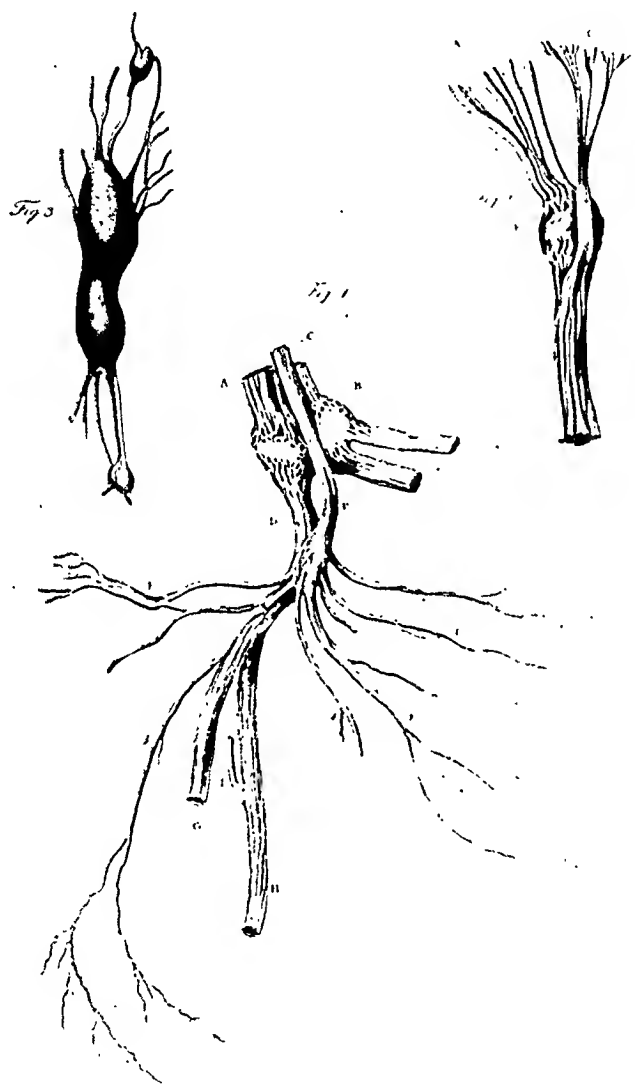
\* Authors who have treated of the anatomy of the ganglions, have not distinguished between the two classes of ganglions as belonging to the sensitive and sympathetic systems of nerves.

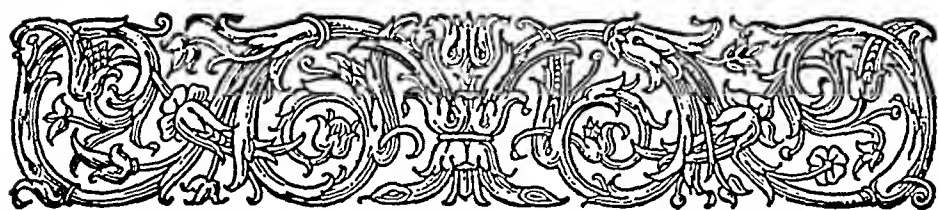


### BELL'S PHENOMENON

The following paper, *On the motions of the eye, in illustration of the uses of the muscles and nerves of the orbit*, is the earliest reference I find to a description by Charles Bell of the outward and upward rolling of the eyeball on an attempt to close the eye (Bell's phenomenon). This paper was presented before the Royal Society of London in 1823, and thus precedes Bell's paper on facial palsy by six years. The paper here given is a beautiful example of the correlation between anatomic and clinical investigation for the advancement of medical knowledge.







# XV. On the Motions of the Eye in Illustration of the Uses of the Muscles and Nerves of the Orbit

BY

CHARLES BELL, ESQ.

Communicated by Sir Humphry Davy, Bart. P.R.S.

Read March 20, 1823

**T**HE object of this paper is to explain the reason of there being six nerves distributed to the eye, and consequently crowded into the narrow space of the orbit.

But before it is possible to assign the uses of these nerves, we must examine the motions of the eye more minutely than has hitherto been done, and try to comprehend the offices to be performed. Much as the eye has been studied, the frame-work which suspends it, and by which it is moved and protected, has not received the attention it deserves. Yet this frame-work, or apparatus, is not less calculated to renew our wonder, than the properties of the organ itself.

It is therefore necessary to divide the paper into two parts. First, to show the uses of the apparatus which is exterior to the eye-ball; and then, in the second place, to consider how the nerves minister to these offices.

## PART I

OF THE MUSCLES AND FRAME-WORK WHICH ARE AROUND THE  
EYE-BALL

Even grave and learned men have eulogized this organ as the most necessary to intellectual enjoyment, and which ranges from the observation of the fixed stars, to that of the expression in the human face. But this admiration is in part misplaced, if given to the optic nerve and ball of the eye exclusively; since these high endowments belong to the exercise of the whole eye, its exterior apparatus as much as to that nerve which is sensible to the impressions of light. It is to the muscular apparatus, and to the conclusions we are enabled to draw from the consciousness of muscular effort, that we owe that geometrical sense, by which we become acquainted with the form, and magnitude, and distance of objects. We might as well expect to understand the uses of a theodolite, or any complicated instrument for observations, by estimating the optical powers of the glasses, without considering the quadrant, level, or plumb-line, as expect to learn the whole powers of the eye by confining our study to the naked ball. I propose to show, that we must distinguish the motions of the eye, according to their objects or uses, whether for the direct purpose of vision, or for the preservation of the organ: that the eye undergoes a revolving motion not hitherto noticed; that it is subject to a state of rest and activity, and that the different conditions of the retina are accompanied by appropriate conditions of the surrounding muscles; that these muscles are to be distinguished into two natural classes; and that in sleep, faintness, and insensibility, the eye-ball is given up to the one, and in watchfulness, and the full exercise of the organ, it is given up to the influence of the other class of muscles: and finally, that the consideration of these natural conditions of the eye explains its changes as symptomatic of disease, or as expressive of passion.

## MOTIONS OF THE EYE-BALL AND EYE-LIDS

Two objects are obtained through the motion of the eye-ball. First, the controul and direction of the eye to objects; secondly,

the preservation of the organ itself, either by withdrawing the surface from injury, or by the removal of what is offensive to it. Without keeping this distinction before us, we shall not easily discover the uses of the parts.

There is a motion of the eye-ball, which, from its rapidity, has escaped observation. At the instant in which the eye-lids are closed, the eye-ball makes a movement which raises the cornea under the upper eye-lid.

If we fix one eye upon an object, and close the other eye with the finger in such a manner as to feel the convexity of the cornea through the eye-lid, when we shut the eye that is open, we shall feel that the cornea of the other eye is instantly elevated; and that it thus rises and falls in sympathy with the eye that is closed and opened. This change of the position of the eye-ball takes place during the most rapid winking motions of the eye-lids. When a dog was deprived of the power of closing the eye-lids of one eye by the division of the nerve of the eye-lids, the eye did not cease to turn up when he was threatened, and when he winked with the eye-lids of the other side.

Nearly the same thing I observed in a girl whose eye-lids were attached to the surrounding skin, owing to a burn; for the fore part of the eye-ball being completely uncovered, when she would have winked, instead of the eye-lids descending, the eye-balls were turned up, and the cornea was moistened by coming into contact with the mouths of the lacrymal ducts.

The purpose of this rapid insensible motion of the eye-ball will be understood on observing the form of the eye-lids and the place of the lacrymal gland. The margins of the eye-lids are flat, and when they meet, they touch only at their outer edges, so that when closed there is a gutter left between them and the cornea. If the eye-ball were to remain without motion, the margins of the eye-lids would meet in such a manner on the surface of the cornea, that a certain portion would be left untouched, and the eye would have no power of clearing off what obscured the vision, at that principal part of the lucid cornea which is in the very axis of the eye; and if the tears flowed they would be left accumulated on the centre of the cornea, and

winking, instead of clearing the eye, would suffuse it. To avoid these effects, and to sweep and clear the surface of the cornea, at the same time that the eye-lids are closed, the eye-ball revolves, and the cornea is rapidly elevated under the eye-lid.

Another effect of this motion of the eye-ball is to procure the discharge from the lacrymal ducts; for by the simultaneous ascent of the cornea, and the descent of the upper eye-lid, the membrane on which the ducts open is stretched, and the effect is like the elongation of the nipple, facilitating the discharge of tears.

By the double motion, the descent of the eye-lid and the ascent of the cornea at the same time, the rapidity with which the eye escapes from injury is increased. Even creatures which have imperfect eye-lids, as fishes, by possessing this rapid revolving motion of the eye, avoid injury and clear off impurities.

I may observe in passing, that there is a provision for the preservation of the eye, in the manner in which the eye-lids close, which has not been noticed; while the upper eye-lid falls, the lower eye-lid is moved towards the nose. This is a part of that curious provision for collecting offensive particles towards the inner corner of the eye. If the edges of the eye-lids be marked with black spots, it will be seen that when the eye-lids are opened and closed, the spot on the upper eye-lid will descend and rise perpendicularly, while the spot on the lower eye-lid will play horizontally like a shuttle.

To comprehend certain actions of the muscles of the eye, we must remember that the caruncle and membrane called semilunaris, seated in the inner corner of the eye, are for ridding the eye of extraneous matter, and are in fact, for the same purpose with that apparatus which is more perfect and appropriate in beasts and birds.

The course of our enquiry makes some observation of these parts necessary.

In quadrupeds there is a gland for secreting a glutinous and adhesive fluid, which is seated on that side of the orbit next the nose; it is quite distinct from the lacrymal gland; it is squeezed by an apparatus of muscles, and the fluid exudes upon the

surface of the third eye-lid. This third eye-lid is a very peculiar part of the apparatus of preservation. It is a thin cartilage, the posterior part of which is attached to an elastic body. This body is lodged in a division or depression of the orbit on the side towards the nose. When the eye is excited, the eye-ball is made to press on the elastic body and force it out of its recess or socket; the consequence of which is the protrusion of the cartilaginous third eye-lid, or haw, as it is termed in the horse. By this mechanism the third eye-lid is made to sweep rapidly over the surface of the cornea, and by means of the glutinous fluid with which its surface is bedewed, it attaches and clears away offensive particles.

In birds, the eye is an exquisitely fine organ, and still more curiously, and as we might be tempted to say, artificially protected. The third eye-lid is more perfect; it is membranous and broad, and is drawn over the surface of the eye by means of two muscles which are attached to the back part of the eye-ball, and by a long round tendon, that makes a course of nearly three parts of the circumference of the ball. The lacrymal gland is small, and seated low, but the mucous gland is of great size, and seated in a cavity deep and large, and on the inside of the orbit. As the third eye-lid is moved by an apparatus which cannot squeeze the mucous gland at the same time that the eye-lid is moved, as in quadrupeds, the oblique muscles are particularly provided to draw the eye-ball against the gland, and to force out the mucus on the surface of the third eye-lid. It flows very copiously; and this is probably the reason of the smallness of the proper lacrymal gland which lies on the opposite side of the orbit.

We already see two objects attained through the motion of these parts: the moistening the eye with the clear fluid of the lacrymal gland, and the extraction or protrusion of offensive particles.

There is another division of this subject no less curious; the different conditions of the eye during the waking and sleeping state, remain to be considered. If we approach a person in disturbed sleep when the eye-lids are a little apart, we shall not



see the pupil nor the dark part of the eye, as we should were he awake, for the cornea is turned upwards under the upper eye-lid. If a person be fainting, as insensibility comes over him the eyes cease to have speculation; that is they want direction, and are vacant, and presently the white part of the eye is disclosed by the revolving of the eye-ball upwards. So it is on the approach of death; for, although the eye-lids be open, the pupils are in part hid, being turned up with a seeming agony, which however is the mark of encreasing insensibility.

It will now be admitted that the variety of motions to which the eye is subjected, require the complication of muscles which we find in the orbit, and it must be obvious to the most casual observer, that unless these various offices and different conditions of the eye be considered, it will be in vain to attempt an accurate classification of the muscles of the orbit.

#### OF THE ACTIONS OF THE MUSCLES OF THE EYE, AND THEIR NATURAL CLASSIFICATION

The muscles attached to the eye-ball are in two classes, the recti and obliqui. The recti muscles are four in number, and comes from the bottom of the orbit, and run a straight course forwards and outwards; they embrace the eye-ball, and are inserted at four cardinal points into it. The obliqui are two muscles having a direction backwards and outwards;\* they embrace the eye-ball, one passing over it obliquely, the other under it obliquely.

That the recti muscles perform the office of directing the axis of the eye, turning it round to every point in the sphere of vision, there are many proofs. In the first place, their origin, course, and insertion, accurately fit them for this office; and they are obviously equal to it, unassisted by other muscles. In the next place, from man down to the cuttle-fish, the voluntary motions of the eye are the same, and the origin, course, and insertion of these muscles are similar, while the other muscles vary with the change of apparatus which is around the eye.

\* We may say so, for although the superior oblique muscle comes from the back of the orbit, yet, by passing through the trochea, it has a course backwards and outwards to its insertion.

The oblique muscles of the eye stand contrasted with the recti in every respect, in number, size, and direction. Yet it is a received opinion, that they antagonize the recti, and keep the eye suspended. To this opinion there are many objections.

1. In creatures where the eye is socketed on a cup of cartilage and cannot retract, the oblique muscles are nevertheless present.

2. Where a powerful retractor muscle is bestowed in addition to the recti muscles, the oblique muscles have no additional magnitude given to them.

3. In matter of fact, the human eye cannot be retracted by the united action of the recti as we see quadrupeds draw in their eyes, which is an argument against these muscles being retractors, and therefore against the obliqui being their opponents, to draw it forward.

To these, other objections, no less strong, may be added. We have just found that certain very rapid motions are to be performed by the eye-ball; now it can be demonstrated, that a body will be moved in less time by a muscle which is oblique to the line of motion, than if it lay in the line on which the body moves. If the oblique muscles were either opponents or coadjutors of the recti, there appears no reason why they should be oblique, but the contrary; for as the points of their insertion must move more rapidly than those of the recti, they are unsuitable. On the other hand, that there may be no difference in the time of the action and relaxation of the several classes, we see a reason why one rectus should be opposed by another, and why there being occasion for one oblique its antagonist should also be oblique.

In proportion as a muscle gains velocity by its obliquity, it loses power; from the obliquity, therefore, of these muscles believed to be opposed to the recti, and from their being two of them to four of the latter, they are disproportioned in strength, and the disproportion proves that the two classes of muscles are not antagonists.

By dissection and experiment it can be proved, that the oblique muscles are antagonists to each other, and that they roll the eye in opposite directions, the superior oblique directing the pupil downwards and outwards, and the inferior oblique direct-

ing it upwards and inwards. But it is proved that any two of the recti muscles are equal to the direction of the pupil in the diagonal between them, and there is no reason why an additional muscle should be given, to direct the pupil upwards and inwards more than upwards and outwards, or downwards and inwards. It is evident then, that the oblique muscles are not for assisting the recti in directing the eye to object, but that they must have some other appropriate office. If we proceed farther, it must be by experiment.

#### EXPERIMENTAL ENQUIRY INTO THE ACTION OF THESE MUSCLES

I. I divided the superior rectus or attollens in a rabbit, and felt something like disappointment on observing the eye remain stationary. Shortly afterwards, on looking to the animal while it was feeding, I saw the pupil depressed, and that the animal had no power of raising it.

The explanation I conceive to be this: during the experiment the eye was spasmodically fixed by the general action of the muscles, and particularly by the powerful retractor, a muscle peculiar to quadrupeds. But on the spasm relaxing, and when the eye was restored to the influence of the voluntary muscles, the recti, the voluntary power of raising the eye being lost by the division of the superior muscle, the eye was permanently depressed.

II. Wishing to ascertain if the oblique muscles contract to force the eye-ball laterally towards the nose, I put a fine thread round the tendon of the superior oblique muscle of a rabbit, and appended a glass bead to it of a weight to draw out the tendon a little. On touching the eye with a feather, I had the pleasure of seeing the bead drawn up. And on repeating the experiment, the thread was forcibly drawn through my fingers.

By experiments made carefully in the dead body, (having distended the eye-ball by dropping mercury into it to give it its full globular figure) I had found that the action of the superior oblique muscle is to turn the pupil downwards and outwards, and that the inferior oblique just reverses this motion of the eye. In the above experiment there is abundance of proof that the

superior oblique muscle acted, and yet the pupil was not turned downwards and outwards, therefore both oblique muscles must have been in action. Their combined action draws the eye-ball towards the nose.

In the violent spasmodic affection of the eye, when it is painfully irritated, I believe that all the muscles, both of the eye-ball and eye-lids, are excited. In quadrupeds, I have ascertained that the oblique muscles act when the haw is protruded, but I have also found that the retractor oculi alone, is capable of forcing forwards the haw.

But quadrupeds having an additional apparatus of muscles to those of the human eye, are not suited for experiments intended to illustrate the motions of our eyes. The monkey has the same muscles of the eye with man.

III. I cut across the tendon of the superior oblique muscle of the right eye of a monkey. He was very little disturbed by this experiment, and turned round his eyes with his characteristic enquiring looks, as if nothing had happened to affect the eye.

IV. I divided the lower oblique muscle of the eye of a monkey. The eye was not, in any sensible manner, affected; the voluntary motions were perfect after the operation.

V. On holding open the eyes of the monkey, which had the superior oblique muscle of the right eye divided, and waving the hand before him, the right eye turned upwards and inwards, while the other eye had a scarcely perceptible motion in the same direction. When the right eye was thus turned up, he seemed to have a difficulty in bringing it down again.

From these experiments it is proved, that the division of the oblique muscles does not in any degree affect the voluntary motions by which the eye is directed to objects.

This cannot however be said of the involuntary winking motions of the eyes. We have seen that in winking to avoid injury, the oblique muscles were in operation; and that the inferior oblique muscle gained in the power of elevating the eye-ball by the division of the superior oblique, its opponent.\*

\* Since this paper was read, a case has occurred in the Middlesex Hospital, under the care of my colleague, Dr. Macmichael, which shows the consequences of the eye and eye-

ON THE TWO CONDITIONS OF THE EYE, ITS STATE OF REST AND OF  
ACTIVITY

The eye is subject to two conditions: a state of rest with entire oblivion of sensation, and a state of watchfulness, during which both the optic nerve and the nerve of voluntary motion are in activity. When the eye is at rest, as in sleep, or even when the eye-lids are shut, the sensation on the retina being then neglected, the voluntary muscles resign their office, and the involuntary muscles draw the pupil under the upper eye-lid. This is the condition of the organ during perfect repose.

On the other hand, there is an inseparable connection between the exercise of the sense of vision and the exercise of the voluntary muscles of the eye. When an object is seen, we enjoy two senses; there is an impression upon the retina; but we receive also the idea of position or relation which it is not the office of the retina to give. It is by the consciousness of the degree of effort put upon the voluntary muscles, that we know the relative position of an object to ourselves. The relation existing between the office of the retina and of the voluntary muscles, may be illustrated in this manner.

Let the eyes be fixed upon an illuminated object until the retina be fatigued, and in some measure exhausted by the image, then closing the eyes, the figure of the object will continue present to them: and it is quite clear that nothing can change the

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lids being rendered immovable. In this case the surface of the eye is totally insensible, and the eye remains fixed, and directed straight forwards, whilst the vision is entire. The outward apparatus being without sensibility and motion, and the surface not cleared of irritating particles, inflammation has taken place, and the cornea is becoming opaque; thus proving the necessity of the motions of the eye to the preservation of the organ. Another curious circumstance, illustrative of the observations made above, is, that when both eyes are shut, the eye affected continues to be sensible of a red light coming through the eye-lid, whilst the sound eye is in darkness. The reason of this I apprehend to be: the eye which possesses its natural motions is turned up, but the eye which continues fixed, looking forwards, receives the light through the transparent eye-lid; and thus it appears that the dropping of the eye-lid would make an imperfect curtain, if unaccompanied by the turning up of the eye-ball during repose.

The interest of this case will be increased by the considerations in the Second Part of this Paper.

place of this impression on the retina. But notwithstanding that the impression on the retina cannot be changed, the idea thence arising may. For by an exertion of the voluntary muscles of the eye-ball, the body seen will appear to change its place, and it will, to our feeling, assume different positions according to the muscle which is exercised. If we raise the pupil, we shall see the body elevated, or if we depress the pupil, we shall see the body placed below us; and all this takes place while the eye-lids are shut, and when no new impression is conveyed to the retina. The state of the retina is here associated with a consciousness of muscular exertion; and it shows that vision in its extended sense is a compound operation, the idea of position of an object having relation to the activity of the muscles.

We may also show, by varying this experiment, that an agitated state of the muscles, or a state of action where the muscles are at variance or confused, affects the idea of the image. If we look on the luminous body so as to make this impression on the retina, and then cover the face so as to exclude the light, keeping the eye-lids open, and if we now squint, or distort the eyes, the image which was vividly impressed upon the retina instantly disappears as if it were wiped out. Does not this circumstance take place, because the condition of the muscles thus unnaturally produced, being incongruous with the exercise of the retina, disturbs its operation?

If we move the eye by the voluntary muscles, while this impression continues on the retina, we shall have the notion of place or relation raised in the mind; but if the motion of the eye-ball be produced by any other cause, by the involuntary muscles, or by pressure from without, we shall have no corresponding change of sensation.

If we make the impression on the retina in the manner described, and shut the eyes, the image will not be elevated, although the pupils be actually raised, as it is their condition to be when the eyes are shut, because there is here no sense of voluntary exertion. If we sit at some distance from a lamp which has a cover of ground glass, and fix the eye on the centre of it, and then shut the eye and contemplate the phantom in the

eye; and if, while the image continues to be present of a fine blue colour, we press the eye aside with the finger, we shall not move that phantom or image, although the circle of light produced by the pressure of the finger against the eye-ball moves with the motion of the finger.

May not this be accounted for in this manner: the motion produced in the eye-ball not being performed by the appropriate organs, the voluntary muscles, it conveys no sensation of change to the sensorium, and is not associated with the impression on the retina, so as to affect the idea excited in the mind? It is owing to the same cause that, when looking on the lamp, by pressing one eye, we can make two images, and we can make the one move over the other. But, if we have received the impression on the retina so as to leave the phantom visible when the eye-lids are shut, we cannot, by pressing one eye, produce any such effect. We cannot, by any degree of pressure, make that image appear to move, but the instant that the eye moves by its voluntary muscles, the image changes its place; that is, we produce the two sensations necessary to raise this idea in the mind; we have the sensation on the retina combined with the consciousness or sensation of muscular activity.

These experiments and this explanation of the effect of the associated action of the voluntary muscles of the eye-ball, appear to me to remove an obscurity in which this subject has been left by the latest writers. In a most scientific account of the eye and of optics, lately published, it is said on this question, "we know nothing more than that the mind residing, as it were, in every point of the retina, refers the impression made upon it, at each point, to a direction coinciding with the latest portion of the ray which conveys the impression." The same author says "Kepler justly ascribed erect vision from an inverted image to an operation of the mind by which it traces the rays back to the pupil, and thus refers the lower part of the image to the upper side of the eye." What can be here meant by the mind following back the ray through the humors of the eye? It might as well follow the ray out of the eye, and like the spider feel along the lines. A much greater authority says we puzzle our-

selves without necessity. "We call that the lower end of an object which is next the ground." No one can doubt that the obscurity here, is because the author has not given himself room to illustrate the subject by his known ingenuity and profoundness. But it appears to me, that the utmost ingenuity will be at a loss to devise an explanation of that power by which the eye becomes acquainted with the position and relation of objects, if the sense of muscular activity be excluded, which accompanies the motion of the eye-ball.

Let us consider how minute and delicate the sense of muscular motion is by which we balance the body, and by which we judge of the position of the limbs, whether during activity or rest. Let us consider how imperfect the sense of touch would be, and how little of what is actually known through the double office of muscles and nerves, would be attained by the nerve of touch alone, and we shall be prepared to give more importance to the recti muscles of the eye, in aid of the sense of vision: to the offices performed by the frame around the eye-ball in aid of the instrument itself.

#### OF THE EXPRESSION OF THE EYE, AND OF THE ACTIONS OF THE OBLIQUE MUSCLES IN DISEASE

If, as I have alleged, the uses of the oblique muscles of the eye have been misunderstood, and if, as I hope presently to prove, the distinctions of the nerves have been neglected, the symptoms of disease, and the sources of expression in the eye, must remain to be explained.

During sleep, in oppression of the brain, in faintness, in debility after fever, in hydrocephalus, and on the approach of death, the pupils of the eyes are elevated. If we open the eye-lids of a person during sleep or insensibility, the pupils will be found elevated. Whatever be the cause of this, it will be found that it is also the cause of the expression in sickness and pain, and exhaustion, whether of body or mind: for then the eye-lids are relaxed and fallen, and the pupils elevated so as to be half covered by the upper eye-lid. This condition of the eye during its insensible unexercised state, we are required to explain.



It is a fact familiar to pathologists, that when debility arises from affection of the brain, the influence is greatest on those muscles which are, in their natural condition, most under the command of the will. We may perceive this in the progressive stages of debility in the drunkard, when successively the muscles of the tongue, the eyes, the face, the limbs, become unmanageable; and, under the same circumstances, the muscles which have a double office, as those of the chest, lose their voluntary motions, and retain their involuntary motions, the force of the arms is gone long before the action of breathing is affected.

If we transfer this principle, and apply it to the muscles of the eye, we shall have an easy solution of the phenomena above enumerated. The recti are voluntary muscles, and they suffer debility before the oblique muscles are touched by the same condition; and the oblique muscles prevailing, roll the eye.

If it be farther asked, why does the eye roll upwards and inwards? We have to recollect, that this is the natural condition of the eye, its position when the eye-lids are shut and the light excluded, and the recti at rest and the obliqui balanced.

Although I am aware that medical histories do not often lead to the improvement of strict science, yet I am tempted to describe the condition of a patient now under my care, because it exhibits a succession of those phenomena which we seek to explain. He presented himself to me in the hospital, with a distinct squint, the left eye being distorted from the object. On the eye-lid of the right eye there was a deep and open ulcer; the man was in danger of losing the right eye, and required prompt assistance; but before he could be brought under the influence of medicine, the inflamed sore became deeper and the cornea opaque. The superior rectus muscle being, as I suppose, injured by the encreasing depth of the sore, the pupil became permanently depressed. The sight of the right eye being now lost, the left eye came into use; it was directed with precision to objects, he had no difficulty in using it, and it daily became stronger.

After a few weeks, medicine having had its influence, the sore on the upper eye-lid of the right eye healed, the inflammation and opacity of the eye gradually diminished, the light became

again visible to him; first it was yellow, and then a deep purple. And now the muscles resumed their influence, and the eye was restored to parallel motion with the other, and so as considerably to embarrass the vision. But the inflammation of the upper eye-lid had been so great, as considerably to diminish its mobility; and what appeared most extraordinary, the lower eye-lid assumed the office of the upper one, and a very unusual degree of motion was remarked in it. It was depressed when he attempted to open the eye, and elevated and drawn towards the nose, when he closed the eye. But the upper eye-lid was not only stiff, but diminished in breadth; so that notwithstanding the remarkable elevation of the lower eye-lid, their margins were not brought together, and we could perceive the motion of the eye-ball; in his attempt to close the eye we saw the pupil elevated, and the white part of the eye exposed.

I shall now attempt the explanation of some of these phenomena:

The impression upon the left eye had been weak from infancy, and the retina being unexercised, the recti or voluntary muscles wanted their excitement, and were deficient in activity; the involuntary muscles therefore prevailed, and the pupil was turned upwards and inwards, and consequently removed from the axis of the other eye. But when that other eye became obscured, the left eye being the only inlet to sensation, the attention became directed to the impression on the retina, the voluntary muscles were excited to activity, and they brought the eye to bear upon objects. This eye improved daily, because the natural exercise of a part is its stimulus to perfection, both in function and in growth. When the right eye became transparent and the light was admitted, the voluntary muscles of that eye partook of their natural stimulus, and commenced that effort in search of the object, which in the course of a few days brought the eye to its proper axis, and both eyes to parallelism.

The next thing that attracts our attention in this short narrative, is the revolving of the eye-ball. It has been explained in a former part of the paper, that when the eye-lids are shut, the recti or voluntary muscles resign their office, and the inferior

oblique muscle gains power, and the eye-ball traverses so as to raise the pupil. It will not have escaped observation, that the pupil of this eye was depressed, and could not be elevated for the purpose of vision, owing, as we have supposed, to the injury of the rectus attollens, at the same time that it was thus raised involuntarily, in the attempt to shut the eye; a proof that this insensible motion is performed by the lower oblique muscle, and not the superior rectus muscle.

The circumstance of the lower eye-lid assuming the functions of the upper one, and moving like the lower eye-lid of a bird, reminds me of an omission in the account of authors. They have sought for a depressor of the inferior eye-lid, which has no existence, and is quite unnecessary; for the motion of the *M. elevator palpebrae superioris* opens wide the eye-lids, and depresses the lower eye-lid, at the same time that it elevated the upper eye-lid. If we put the finger on the lower eye-lid when the eye is shut, and then open the eye, we shall feel that during this action the eye-ball is pushed outwards; and we may observe, that the lower eye-lid is so adapted as to slip off the convex surface of the ball, and is consequently depressed. The reason of this is, that the muscle which raises the upper eye-lid passes over a considerable part of the upper and back part of the eye-ball, and the origin and insertion of the muscle being under the highest convexity of the ball, that body must be pressed forwards in proportion to the resistance of the upper eye-lid to rise. In the preceding case the upper eye-lid being stiff and unyielding, both the origin and the insertion of the *elevator palpebrae* became fixed points; consequently, the action of the muscle fell entirely on the eye-ball itself, whereby it was forced downwards and forwards in an unusual manner, and so depressed the lower eye-lid to an unusual degree. Thus the muscle became a depressor of the inferior eye-lid, instead of an elevator of the upper eye-lid! The motion of elevation in the lower eye-lid was of course performed by an encreased action of the lower portion of the *orbicularis palpebrarum*.

The Author has to regret that these minute circumstances regarding the action of the muscles of the eye have led him to

so great a length; he hopes they are not altogether without interest in themselves, while the discussion will afford him secure ground for establishing an arrangement of the nerves of the eye, and will enable him to distinguish them according to their uses.

## EXPLANATION OF PLATE XXI

## FIG. 1. THE MUSCLES OF THE EYE SEEN IN FRONT

A. B. C. D. The recti muscles; voluntary muscles.

E. The superior oblique muscle or trochlearis.

a. The trochlea cut off from the bone and left attached to the tendon. It is a loop through which the tendon runs.

b. The tendon of the trochlearis muscle expanding and running to its insertion.

G. The inferior oblique muscle. It is seen, like the tendon of the superior oblique, to run backwards and outwards.

## FIG. 2. THE MUSCLES OF THE EYE SEEN IN PROFILE

A. B. D. Three of the recti muscles. They arise together from the periosteum of the bottom of the orbit, and are inserted into the anterior part of the sclerotic coat of the eye.

E. The superior oblique muscle, or trochlearis.

a. The trochlea.

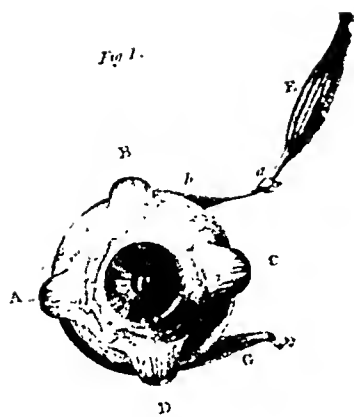
b. The reflected tendon inserted into the back and outer part of the sclerotic coat.

G. The inferior oblique muscle.

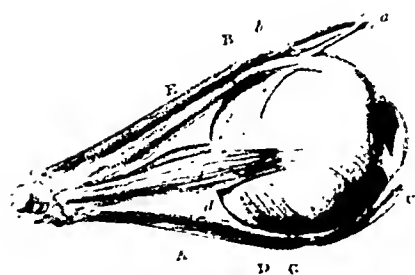
c. Its origin from the anterior part of the orbit.

d. Its insertion into the back and outer part of the eye-ball.

*Fig 1.*



*Fig 2*











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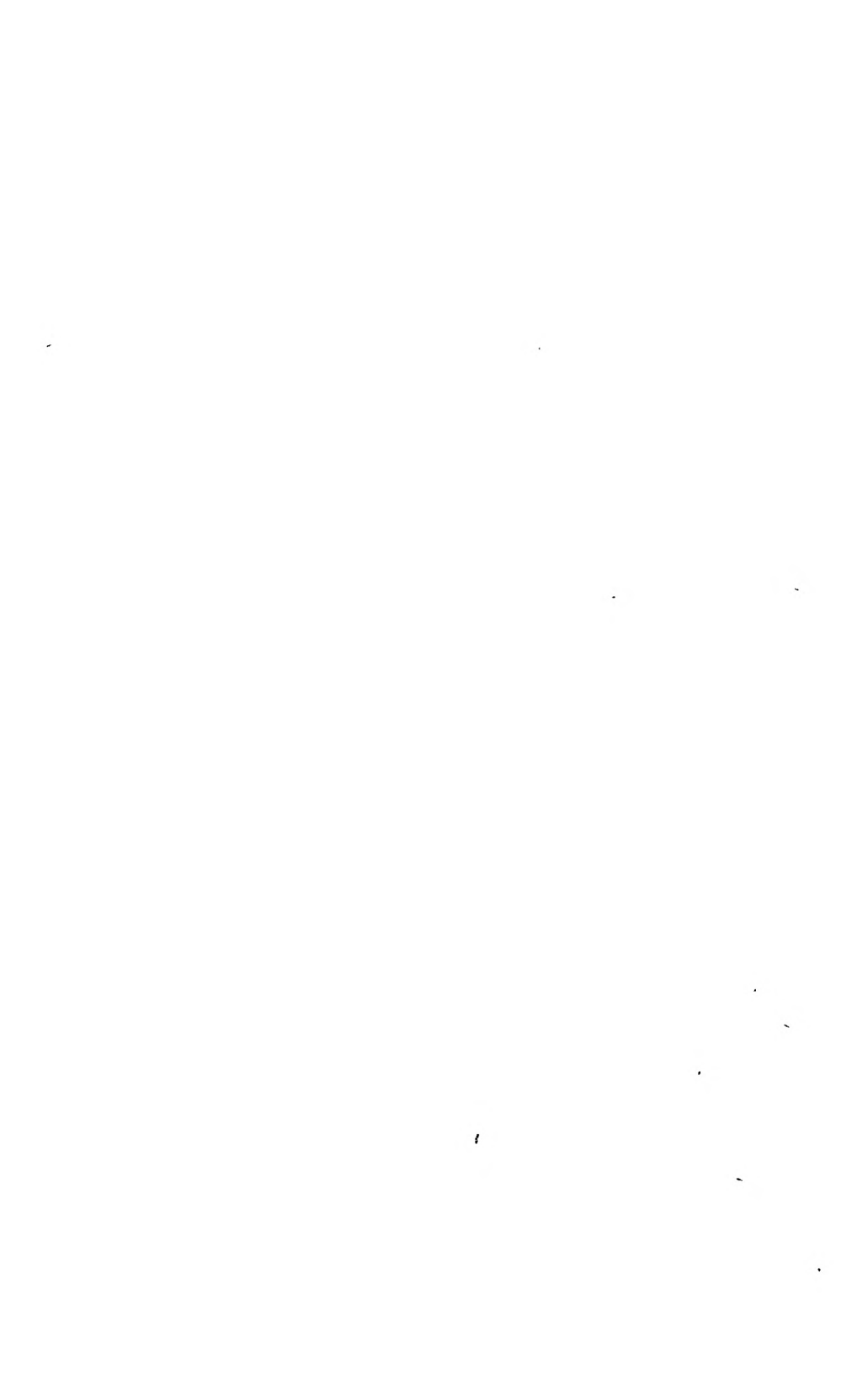
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*Very truly yours  
Oliver Wendell Holmes.*

OLIVER WENDELL HOLMES  
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## Oliver Wendell Holmes

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- 1809 Born August 29, at Cambridge, Massachusetts, the third of five children, son of Reverend Abiel Holmes, a Calvinist preacher. His mother was Sarah Wendell, a descendant of Governor Simon Bradstreet, distinguished in the early history of Massachusetts. Attended school in Cambridgeport.
- 1824 Age 15. Attended Phillips Academy at Andover for one year.
- 1829 Age 20. Graduated from Harvard University with A.B.
- 1830 Age 21. Entered Harvard Law School for one year. In autumn entered Harvard Medical School. Wrote the poem *Old Ironsides*.
- 1833 Age 24. Went to Europe to continue medical studies for two years. Spent most of the time in Paris, worked under Louis at La Pitié.
- 1836 Age 27. Became M.D. at Harvard. Joined Massachusetts Medical Society.
- 1838 Age 29. Appointed Professor of Anatomy and Physiology in Dartmouth College at Hanover, N. H. Held the position for two years.
- 1840 Age 31. Married Amelia Lee Jackson, daughter of Hon. Charles Jackson, for eleven years a judge of the Massachusetts Supreme Court. Had two sons and one daughter.
- 1843 Age 34. Published *The Contagiousness of Puerperal Fever*.
- 1847 Age 38. Appointed Parkman Professor of Anatomy and Physiology in Harvard Medical School. Held the

position for thirty-eight years. Was also dean of Harvard Medical School until 1853.

- 1857 Age 48. Began essays entitled *The Autocrat of the Breakfast-Table*, followed by other titles in the same series.
- 1863 Age 54. University Lecturer for one year.
- 1876 Age 67. Overseer of Harvard College until 1882.
- 1880 Age 71. LL.D. from Harvard.
- 1882 Age 73. Professor of Anatomy, Emeritus.
- 1886 Age 77. LL.D. from Edinburgh, Litt.D. from Cambridge, D.C.L. from Oxford.
- 1889 Age 80. A.M. (Hon.) from Harvard.
- 1894 Age 85. Died October 17, painlessly, while sitting in his chair. Services in King's Chapel, buried in Mount Auburn Cemetery.

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## HOLMES AND PUERPERAL FEVER

In 1843, at the age of 34, Oliver Wendell Holmes wrote a paper, *On the Contagiousness of Puerperal Fever*, which is a mile-post in the history of medicine and in the attitude of physicians toward infection. The paper was written for the Boston Society for Medical Improvement and published in a journal which ceased to exist after the first year. Because of its small circulation and the storm of controversy aroused, Holmes republished the paper in 1855. On the ensuing pages the original essay is reproduced in its entirety and the Introduction to the book of 1855 follows.

Holmes tells us that he was prompted to write the essay because of "the discussion—suggested by a case, reported at the preceding meeting, of a physician who made an examination of the body of a patient who had died with puerperal fever, and who himself died in less than a week, apparently in consequence of a wound received at the examination, having attended several women in confinement in the mean time, all of whom, as alleged, were attacked with puerperal fever." Holmes desired to gather together all the information available from older, more experienced practitioners and to arrive at a conclusion as to the cause and course of this dreadful disease.

Puerperal fever has been recognized from the earliest days of medicine. Hippocrates described a typical case in *The Epidemics*, Book 1, Sec. 3, Ch. 13, Case 4. Both he and Galen thought the disease due to retention of lochia and decomposition of remnants of placenta. Garrison says that the condition was first defined and differentiated by Willis in *De Febris*, 1660, Ch. 16. Malouin noted the disease at the Hotel Dieu in 1746 and Gordon described it in Aberdeen in 1795. Likewise in the 18th century, Charles White of Manchester, England, recognized the contagion and recommended scrupulous cleanliness and Thomas Denman of England realized the disease was transmitted from one patient to another by midwives and nurses.

At the exact time Holmes in Boston was collecting material for his essay, in far-off Vienna, at the Lying-In Hospital, a young assistant, Ignaz Philipp Semmelweis, was impressed by the higher mortality of delivered women in the wards than in homes.

Neither man knew of the other's work. Semmelweis' inquiring mind fixed upon the association of students returning from the postmortem rooms to the wards and the direct transmission of infectious material. He accordingly ordered hands washed in chlorine water and was able to report a reduction of from 10 per cent to 1 per cent in mortality on his wards. But his short-sighted associates could not see that he had hit the bull's-eye of clinical investigation. Semmelweis died in an asylum but his work has made his name known throughout the entire world. Hungary has signally honored this man by removing his ashes from Vienna and burying them with ceremony in Budapest, by placing a tablet on the house in which he was born and by erecting, in one of the great public squares in Budapest, a fine monument which was unveiled at a great international gathering of obstetricians.

How sad that America has not honored Holmes as he deserves! It is hoped that even yet some great public testimonial will take shape and be born for all posterity to gaze upon and for youth to possess as a model to arouse imitation and emulation of this man.

Even after Holmes had brought forth strong proof of the contagiousness of puerperal fever, his views were not readily accepted. In 1850 Trousseau wrote, "the disease had its origin in lesions of the genital tract which were complicated by general secondary lesions, the outcome of puerperal infection." Holmes was severely attacked by the leading obstetricians of Philadelphia, Hodge and Meigs, who believed that irregularity of diet, a confined state of the bowels or atmospheric changes were responsible for the disease. Professor Meigs wrote in 1852, "I prefer to attribute them to accident, or Providence, of which I can form a conception, rather than to a contagion of which I cannot form any clear idea, at least as to this particular malady." Holmes answered Meigs in the Introduction to the publication of 1855 which he tells us was written chiefly for the immature minds of medical students. It is, however, a masterpiece of medical literature which every physician should know.



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# The Contagiousness of Puerperal Fever

BY

OLIVER W. HOLMES, M.D.

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Read before the Boston Society for Medical Improvement, and published by request of the Society

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**I**N COLLECTING, enforcing and adding to the evidence accumulated upon this most serious subject, I would not be understood to imply that there exists a doubt in the mind of any well-informed member of the medical profession as to the fact that puerperal fever is sometimes communicated from one person to another, both directly and indirectly. In the present state of our knowledge upon this point I should consider such doubts merely as a proof that the sceptic had either not examined the evidence, or, having examined it, refused to accept its plain and unavoidable consequences. I should be sorry to think with Dr. Rigby, that it was a case of "oblique vision;" I should be unwilling to force home the *argumentum ad hominem* of Dr. Blundell, but I would not consent to make a *question* of a momentous fact, which is no longer to be considered as a subject for trivial discussions, but to be acted upon with silent promptitude. It signifies nothing that wise and experienced practitioners have sometimes doubted the reality of the danger in question; no man has the right to doubt it any longer. No negative facts, no opposing opinions, be they what they may or whose

they may, can form any answer to the series of cases now within the reach of all who choose to explore the records of medical science.

If there are some who conceive that any important end would be answered by recording such opinions, or by collecting the history of all the cases they could find in which no evidence of the influence of contagion existed, I believe they are in error. Suppose a few writers of authority can be found to profess a disbelief in contagion—and they are very few compared with those who think differently—is it quite clear that they formed their opinions on a view of all the facts, or is it not apparent that they relied mostly on their own solitary experience? Still further, of those whose names are quoted, is it not true that scarcely a single one could by any possibility have known the half or the tenth of the facts bearing on the subject which have reached such a frightful amount within the last few years? Again, as to the utility of negative facts, as we may briefly call them,—instances, namely, in which exposure has not been followed by disease,—although, like other truths, they may be worth knowing, I do not see that they are like to shed any important light upon the subject before us. Every such instance requires a good deal of circumstantial explanation before it can be accepted. It is not enough that a practitioner, should have had a single case of puerperal fever not followed by others. It must be known whether he attended others while this case was in progress, whether he went directly from one chamber to others, whether he took any, and what precautions. It is important to know that several women were exposed to infection derived from the patient, so that allowance may be made for want of predisposition. Now if of negative facts so sifted there could be accumulated a hundred for every one plain instance of communication here recorded, I trust it need not be said that we are bound to guard and watch over the hundredth tenant of our fold, though the ninety and nine may be sure of escaping the wolf at its entrance. If any one is disposed, then, to take a hundred instances of lives endangered or sacrificed out of those I have mentioned, and make it reasonably clear that within a similar time and compass *ten thousand* escaped the same

exposure, I shall thank him for his industry, but I must be permitted to hold to my own practical conclusions, and beg him to adopt or at least to examine them also. Children that walk in calico before open fires are not always burned to death; the instances to the contrary may be worth recording; but by no means if they are to be used as arguments against woolen frocks and high fenders.

I am not sure that this paper will escape another remark which it might be wished were founded in justice. It may be said that the facts are too generally known and acknowledged to require any formal argument or exposition, that there is nothing new in the positions advanced, and no need of laying additional statements before the profession. But on turning to two works, one almost universally, and the other extensively appealed to as authority in this country, I see ample reason to overlook this objection. In the last edition of Dewees's *Treatise on the Diseases of Females*, it is expressly said, "In this country, under no circumstance that puerperal fever has appeared hitherto, does it afford the slightest ground for the belief that it is contagious." In the "*Philadelphia Practice of Midwifery*" not one word can be found in the chapter devoted to this disease, which would lead the reader to suspect that the idea of contagion had ever been entertained. It seems proper, therefore, to remind those who are in the habit of referring to these works for guidance, that there may possibly be some sources of danger they have slighted or omitted, quite as important as a trifling irregularity of diet, or confined state of the bowels, and that whatever confidence a physician may have in his own mode of treatment, his services are of questionable value whenever he carries the bane as well as the antidote about his person.

The practical point to be illustrated is the following: *The disease known as Puerperal Fever is so far contagious as to be frequently carried from patient to patient by physicians and nurses.*

Let me begin by throwing out certain incidental questions, which without being absolutely essential, would render the subject more complicated, and by making such concessions and



assumptions as may be fairly supposed to be without the pale of discussion.

1. It is granted that all the forms of what is called puerperal fever may not be, and probably are not, equally contagious or infectious. I do not enter into the distinctions that have been drawn by authors, because the facts do not appear to me sufficient to establish any absolute line of demarcation between such forms as may be propagated by contagion, and those which are never so propagated. This general result I shall only support by the authority of Dr. Ramsbotham, who gives as the result of his experience, that the same symptoms belong to what he calls the infectious and the sporadic forms of the disease, and the opinion of Armstrong in his original essay. If others can show any such distinction, I leave it to them to do it. But there are cases enough that show the prevalence of the disease among the patients of a single practitioner when the disease was in no degree epidemic, in the proper sense of the term. I may refer to those of Mr. Robertson and of Dr. Pearson, hereafter to be cited, as examples.

2. I shall not enter into any dispute about the particular *mode* of infection, whether it be by the atmosphere the physician carries about him into the sick chamber, or by the direct application of the virus to the absorbing surfaces with which his hand comes in contact. Many facts and opinions are in favor of each of these modes of transmission. But it is obvious that in the majority of cases it must be impossible to decide by which of these channels the disease is conveyed, from the nature of the intercourse between the physician and the patient.

3. It is not pretended that the contagion of puerperal fever must always be followed by the disease. It is true of all contagious diseases that they frequently spare those who appear to be fully submitted to their influence. Even the vaccine virus, fresh from the subject, fails every day to produce its legitimate effect, though every precaution is taken to ensure its action. This is still more remarkably the case with scarlet fever and some other diseases.

4. It is granted that the disease may be produced and variously modified by many causes besides contagion, and more especially by epidemic and endemic influences. But this is not peculiar to the disease in question. There is no doubt that smallpox is propagated to a great extent by contagion, yet it goes through the same periods of periodical increase and diminution which have been remarked in puerperal fever. If the question is asked how we are to reconcile the great variations in the mortality of puerperal fever in different seasons and places with the supposition of contagion, I will answer it by another question from Mr. Farr's letter to the Registrar-General. He makes the statement that "*five* die weekly of smallpox in the metropolis when the disease is not epidemic"—and adds, "The problem for solution is,—Why do the 5 deaths become 10, 15, 20, 31, 58, 88 weekly, and then progressively fall through the same measured steps?"

5. I take it for granted that if it can be shown that great numbers of lives have been and are sacrificed to ignorance or blindness on this point, no other error of which physicians or nurses may be occasionally suspected will be alleged in palliation of this; but that whenever and wherever they can be shown to carry disease and death instead of health and safety, the common instincts of humanity will silence every attempt to explain away their responsibility.

The treatise of Dr. Gordon, of Aberdeen, was published in the year 1795, being among the earlier special works upon the disease. A part of his testimony has been occasionally copied into other works, but his expressions are so clear, his experience is given with such manly distinctness and disinterested honesty, that it may be quoted as a model which might have been often followed with advantage.

"This disease seized such women only as were visited, or delivered, by a practitioner, or taken care of by a nurse, who had previously attended patients affected with the disease."

"I had evident proofs of its infectious nature, and that the infection was as readily communicated as that of the small-pox or

measles, and operated more speedily than any other infection with which I am acquainted."

"I had evident proofs that every person who had been with a patient in the puerperal fever became charged with an atmosphere of infection, which was communicated to every pregnant woman who happened to come within its sphere. This is not an assertion, but a fact, admitting of demonstration, as may be seen by a perusal of the foregoing table,"—referring to a table of seventy-seven cases, in many of which the channel of propagation was evident.

He adds, "It is a disagreeable declaration for me to mention, that I myself was the means of carrying the infection to a great number of women." He then enumerates a number of instances in which the disease was conveyed by midwives and others to the neighboring villages, and declares that "These facts fully prove, that the cause of the puerperal fever, of which I treat, was a specific contagion, or infection, altogether unconnected with a noxious constitution of the atmosphere."

But his most terrible evidence is given in these words, "I ARRIVED AT THAT CERTAINTY IN THE MATTER, THAT I COULD VENTURE TO FORETELL WHAT WOMAN WOULD BE AFFECTED WITH THE DISEASE, UPON HEARING BY WHAT MIDWIFE THEY WERE TO BE DELIVERED, OR BY WHAT NURSE THEY WERE TO BE ATTENDED, DURING THEIR LYING IN: AND, ALMOST IN EVERY INSTANCE, MY PREDICTION WAS VERIFIED."

Even previously to Gordon, Mr. White of Manchester had said, "I am acquainted with two gentlemen in another town, where the whole business of midwifery is divided betwixt them, and it is very remarkable that one of them loses several patients every year of the puerperal fever, and the other never so much as meets with the disorder"—a difference which he seems to attribute to their various modes of treatment.\*

Dr. Armstrong has given a number of instances in his *Essay on Puerperal Fever*, of the prevalence of the disease among the patients of a single practitioner. At Sunderland, "in all, forty-three cases occurred from the first of January to the first of Octo-

\* On the Management of Lying-in Women, p. 120.

ber, when the disease ceased; and of this number forty were witnessed by Mr. Gregson and his assistant Mr. Gregory, the remainder having been separately seen by three accoucheurs." There is appended to the London edition of this essay, a letter from Mr. Gregson, in which that gentleman says, in reference to the great number of cases occurring in his practice, "The cause of this I cannot pretend fully to explain, but I should be wanting in common liberality if I were to make any hesitation in asserting, that the disease which appeared in my practice was highly contagious, and communicable from one puerperal woman to another." "It is customary among the lower and middle ranks of people to make frequent personal visits to puerperal women resident in the same neighborhood, and I have ample evidence for affirming that the infection of the disease was often carried about in that manner; and, however painful to my feelings, I must in candor declare, that it is very probable the contagion was conveyed, in some instances, by myself, though I took every possible care to prevent such a thing from happening, the moment that I ascertained that the distemper was infectious." Dr. Armstrong goes on to mention six other instances within his knowledge, in which the disease had at different times and places been limited, in the same singular manner, to the practice of individuals, while it existed scarcely if at all among the patients of others around them. Two of the gentlemen became so convinced of their conveying the contagion that they withdrew for a time from practice.

I find a brief notice, in an American Journal, of another series of cases, first mentioned by Mr. Davies, in the Medical Repository. This gentleman stated his conviction that the disease is contagious.

"In the autumn of 1822, he met with twelve cases, while his medical friends in the neighborhood did not meet with any, 'or at least very few.' He could attribute this circumstance to no other cause than his having been present at the examination, after death, of two cases, sometime previous, and of his having imparted the disease to his patients, notwithstanding every precaution."\*

\* Philad. Med. Journal for 1825, p. 408.

Dr. Gooch says, "It is not uncommon for the greater number of cases to occur in the practice of one man, whilst the other practitioners of the neighborhood, who are not more skilful or more busy, meet with few or none. A practitioner opened the body of a woman who had died of puerperal fever, and continued to wear the same clothes. A lady whom he delivered a few days afterwards was attacked with and died of a similar disease; two more of his lying-in patients, in rapid succession, met with the same fate; struck by the thought, that he might have carried contagion in his clothes, he instantly changed them, and met with no more cases of the kind.\* A woman in the country, who was employed as washerwoman and a nurse, washed the linen of one who had died of puerperal fever; the next lying-in patient she nursed, died of the same disease; a third nursed by her met with the same fate, till the neighborhood getting afraid of her, ceased to employ her."†

In the winter of the year 1824 "Several instances occurred of its prevalence among the patients of particular practitioners, whilst others who were equally busy met with few or none. One instance of this kind was very remarkable. A general practitioner, in large midwifery practice, lost so many patients from puerperal fever, that he determined to deliver no more for some time, but that his partner should attend in his place. This plan was pursued for one month, during which not a case of the disease occurred in their practice. The elder practitioner being then sufficiently recovered, returned to his practice, but the first patient he attended was attacked by the disease and died. A physician, who met him in consultation soon afterwards, about a case of a different kind, and who knew nothing of his misfortune, asked him whether puerperal fever was at all prevalent in his neighborhood, on which he burst into tears, and related the above circumstances.

"Among the cases which I saw this season in consultation, four

\* A similar anecdote is related by Sir Benjamin Brodie, of the late Dr. John Clarke. *Lancet*, May 2, 1840.

† An Account of some of the most important Diseases peculiar to Women, p. 4.

occurred in one month in the practice of one medical man, and all of them terminated fatally.”\*

Dr. Ramsbotham asserted, in a lecture at the London Hospital, that he had known the disease spread through a particular district, or be confined to the practice of a particular person, almost every patient being attacked with it, while others had not a single case. It seemed capable, he thought, of conveyance, not only by common modes, but through the dress of the attendants upon the patient.†

In a letter to be found in the London Medical Gazette for Jan., 1840, Mr. Roberton, of Manchester, makes the statement which I here give in a somewhat condensed form.

A midwife delivered a woman on the 4th of December, 1830, who died soon after with the symptoms of puerperal fever. In one month from this date the same midwife delivered thirty women, residing in different parts of an extensive suburb, of which number sixteen caught the disease and all died. These were the only cases which had occurred for a considerable time in Manchester. The other midwives connected with the same charitable institution as the woman already mentioned, are twenty-five in number, and deliver, on an average, ninety women a week, or about three hundred and eighty a month. None of these women had a case of puerperal fever. “Yet all this time this woman was crossing the other midwives in every direction, scores of the patients of the charity being delivered by them in the very same quarters where her cases of fever were happening.”

Mr. Roberton remarks, that little more than half the women she delivered during this month took the fever; that on some days all escaped, on others only one or more out of three or four; a circumstance similar to what is seen in other infectious maladies.

Dr. Blundell says, “Those who have never made the experiment, can have but a faint conception how difficult it is to obtain the exact truth respecting any occurrence in which feelings and interests are concerned. Omitting particulars, then, I content myself with remarking, generally, that from more than one dis-

\* *Ib.* p. 71.

† *Lond. Med. Gaz.* May 2, 1835.

trict I have received accounts of the prevalence of puerperal fever in the practice of some individuals, while its occurrence in that of others, in the same neighborhood, was not observed. Some, as I have been told, have lost ten, twelve, or a greater number of patients, in scarcely broken succession; like their evil genius, the puerperal fever has seemed to stalk behind them wherever they went. Some have deemed it prudent to retire for a time from practice. In fine, that this fever may occur spontaneously, I admit; that its infectious nature may be plausibly disputed, I do not deny; but I add, considerately, that in my own family, I had rather that those I esteemed the most should be delivered, unaided, in a stable, by the manger-side, than that they should receive the best help, in the fairest apartment, but exposed to the vapors of this pitiless disease. Gossiping friends, wet nurses, monthly nurses, the practitioner himself, these are the channels by which, as I suspect, the infection is principally conveyed.”\*

At a meeting of the Royal Medical and Chirurgical Society, Dr. King mentioned that some years since a practitioner at Woolwich lost sixteen patients from puerperal fever in the same year. He was compelled to give up practice for one or two years, his business being divided among the neighboring practitioners. No case of puerperal fever occurred afterwards, neither had any of the neighboring surgeons any cases of this disease.

At the same meeting Mr. Hutchinson mentioned the occurrence of three consecutive cases of puerperal fever, followed subsequently by two others, all in the practice of one accoucheur.†

Dr. Lee makes the following statement. “In the last two weeks of September, 1827, five fatal cases of uterine inflammation came under our observation. All the individuals so attacked had been attended in labor by the same midwife, and no example of a febrile or inflammatory disease of a serious nature occurred during that period among the other patients of the Westminster General Dispensary, who had been attended by the other midwives belonging to that institution.”‡

\* Lect. on Midwifery, p. 395.

† Lancet, May 2, 1840.

‡ Lond. Cyc. of Pract. Med., Art. Fever, Puerperal.

The recurrence of long series of cases like those I have cited, reported by those most interested to disbelieve in contagion, scattered along through an interval of half a century, might have been thought sufficient to satisfy the minds of all inquirers that here was something more than a singular coincidence. But if on a more extended observation, it should be found that the same ominous groups of cases, clustering about individual practitioners, were observed in a remote country, at different times, and in widely separated regions, it would seem incredible that any should be found too prejudiced or indolent to accept the solemn truth knelled into their ears by the funeral bells from both sides of the ocean—the plain conclusion that the physician and the disease entered, hand in hand, into the chamber of the unsuspecting patient.

That each series of cases have been observed in this country, and in this neighborhood, I proceed to show.

In Dr. Francis's Notes to Denman's Midwifery, a passage is cited from Dr. Hosack, in which he refers to certain puerperal cases which proved fatal to several lying-in women, and in some of which the disease was supposed to be conveyed by the accoucheurs themselves.\*

A writer in the N. Y. Medical and Physical Journal for October, 1829, in speaking of the occurrence of puerperal fever, confined to one man's practice, remarks, "We have known cases of this kind occur, though rarely, in New York."

I mention these little hints about the occurrence of such cases, partly because they are the first I have met with in American medical literature, but more especially because they serve to remind us that behind the fearful array of published facts, there lies a dark list of similar events, unwritten in the records of science, but long remembered by many a desolated fireside.

Certainly nothing can be more open and explicit than the account given by Dr. Peirson, of Salem, of the cases seen by him. In the first nineteen days of January, 1829, he had five consecutive cases of puerperal fever, every patient he attended being attacked, and the three first cases proving fatal. In March, of

\* Denman's Midwifery, p. 675, 3d Am. Ed.



the same year, he had two moderate cases; in June, another case, and in July, another, which proved fatal. "Up to this period," he remarks, "I am not informed that a single case had occurred in the practice of any other physician. Since that period I have had no fatal case in my practice, although I have had several dangerous cases. I have attended in all twenty cases of this disease, of which four have been fatal. I am not aware that there has been any other case in the town of distinct puerperal peritonitis, although I am willing to admit my information may be very defective on this point. I have been told of some "mixed cases," and "morbid affections after delivery."\*

In the Quarterly Summary of the Transactions of the College of Physicians of Philadelphia,† may be found some most extraordinary developments respecting a series of cases occurring in the practice of a member of that body.

Dr. Condie called the attention of the Society to the prevalence at the present time, of puerperal fever of a peculiarly insidious and malignant character. "In the practice of one gentleman extensively engaged as an obstetrician, nearly every female he has attended in confinement, during several weeks past, within the above limits," (the southern sections and neighboring districts) "had been attacked by the fever."

"An important query presents itself, the Doctor observed, in reference to the particular form of fever now prevalent. Is it, namely, capable of being propagated by contagion, and is a physician who has been in attendance upon a case of the disease, warranted in continuing, without interruption, his practice as an obstetrician? Dr. C., although not a believer in the contagious character of many of those affections generally supposed to be propagated in this manner, has nevertheless become convinced by the facts that have fallen under his notice, that the puerperal fever now prevailing, is capable of being communicated by contagion. How otherwise can be explained the very curious circumstance of the disease in one district being exclusively confined to the practice of a single physician, a Fellow of this Col-

\* Remarks on Puerperal Fever, pp. 12 and 13.

† For May, June; and July, 1842.

lege, extensively engaged in obstetrical practice—while no instance of the disease has occurred in the patients under the care of any other accoucheur practising within the same district; scarcely a female that has been delivered for weeks past has escaped an attack?”

Dr. Rutter, the practitioner referred to, “observed that after the occurrence of a number of cases of the disease in his practice, he had left the city and remained absent for a week, but on returning, no article of clothing he then wore having been used by him before, one of the very first cases of parturition he attended was followed by an attack of the fever, and terminated fatally; he cannot, readily, therefore, believe in the transmission of the disease from female to female, in the person or clothes of the physician.”

The meeting at which these remarks were made was held on the third of May, 1842. In a letter dated December 20, 1842, addressed to Dr. Meigs, and to be found in the *Medical Examiner*,\* he speaks of “those horrible cases of puerperal fever, some of which you did me the favor to see with me during the past summer,” and talks of his experience in the disease, “now numbering nearly 70 cases, all of which have occurred within less than a twelvemonth past.”

And Dr. Meigs asserts, on the same page, “Indeed, I believe that his practice in that department of the profession, was greater than that of any other gentlemen, which was probably the cause of his seeing a greater number of the cases.” This from a professor of midwifery, who some time ago assured a gentleman whom he met in consultation, that the night on which they met was the eighteenth in succession that he himself had been summoned from his repose,† seems hardly satisfactory.

I must call the attention of the inquirer most particularly to the *Quarterly Report* above referred to, and the letters of Dr. Meigs and Dr. Rutter, to be found in the *Medical Examiner*. Whatever impression they may produce upon his mind, I trust

\* For Jan. 21, 1843.

† *Med. Examiner* for Dec. 10, 1842.

they will at least convince him that there is some reason for looking into this apparently uninviting subject.

At the meeting of the College of Physicians just mentioned, Dr. Warrington stated that a few days after assisting at an autopsy of puerperal peritonitis, in which he laded out the contents of the abdominal cavity with his hands, he was called upon to deliver three women in rapid succession. All of these women were attacked with different forms of what is commonly called puerperal fever. Soon after these he saw two other patients, both on the same day, with the same disease. Of these five patients two died.

At the same meeting, Dr. West mentioned a fact related to him by Dr. Samuel Jackson, of Northumberland. Seven females, delivered by Dr. Jackson in rapid succession, while practising in Northumberland county, were all attacked with puerperal fever, and five of them died. "Women," he said, "who had expected me to attend upon them, now becoming alarmed, removed out of my reach, and others sent for a physician residing several miles distant. These women as well as those attended by midwives, all did well; nor did we hear of any deaths in childbed within a radius of fifty miles, excepting two, and these I afterwards ascertained to have been caused by other diseases." He underwent, as he thought, a thorough purification, and still his next patient was attacked with the disease and died. He was led to suspect that the contagion might have been carried in the gloves which he had worn in attendance upon the previous cases. Two months or more after this he had two other cases. He could find nothing to account for these, unless it were the instruments for giving enemata which had been used in two of the former cases, and were employed by these patients. When the first case occurred, he was attending and dressing a limb extensively mortified from erysipelas, and went immediately to the accouchement with his clothes and gloves most thoroughly imbued with its effluvia. And here I may mention, that this very Dr. Samuel Jackson, of Northumberland, is one of Dr. Dewees's authorities against contagion.

The three following statements are now for the first time given to the public. All of the cases referred to occurred within this State, and two of the three series in Boston and its immediate vicinity.

I. The first is a series of cases which took place during the last spring in a town at some distance from this neighborhood. A physician of that town, Dr. C., had the following consecutive cases.

No. 1,	delivered	March 20,	died	March 24.
2,	"	April 9,	"	April 14.
3,	"	10,	"	" 14.
4,	"	11,	"	" 18.
5,	"	27,	"	May 3.
6,	"	28,	Had some symptoms, recovered.	
7,	"	May 8,	Had some symptoms, also recovered.	

These were the only cases attended by this physician during the period referred to. "They were all attended by him until their termination, with the exception of the patient No. 6, who fell into the hands of another physician on the 2d of May. (Dr. C. left town for a few days at this time.) Dr. C. attended cases immediately before and after the above-named periods, none of which, however, presented any peculiar symptoms of the disease."

About the first of July, he attended another patient in a neighboring village, who died two or three days after delivery.

The first patient, it is stated, was delivered on the 20th of March. On the 19th, Dr. C. made the autopsy of a man who died suddenly, sick only 48 hours; had œdema of the thigh, and gangrene extending from a little above the ankle into the cavity of the abdomen." Dr. C. wounded himself, very slightly, in the right hand during the autopsy. The hand was quite painful the night following, during his attendance on the patient No. 1. He did not see this patient after the 20th, being confined to the house, and very sick from the wound just mentioned, from this time until the third of April.

Several cases of erysipelas occurred in the house where the autopsy mentioned above took place, soon after the examination. There were also many cases of erysipelas in town at the time of the fatal puerperal cases which have been mentioned.

The nurse who laid out the body of the patient No. 3, was taken in the evening of the same day with sore throat and erysipelas, and died in ten days from the first attack.

The nurse who laid out the body of the patient No. 4, was taken on the day following with symptoms like those of this patient, and died in a week, without any external marks of erysipelas.

"No other cases of similar character with those of Dr. C. occurred in the practice of any of the physicians in the town or vicinity at the time. Deaths following confinement have occurred in the practice of other physicians during the past year, but they were not cases of puerperal fever. No post-mortem examinations were held in any of these puerperal cases."

Some additional statements in this letter are deserving of insertion. "A physician attended a woman in the immediate neighborhood of the cases numbered 2, 3 and 4. This patient was confined the morning of March 1st, and died on the night of March 7th. It is doubtful whether this should be considered a case of puerperal fever. She had suffered from canker, indigestion and diarrhœa for a year previous to her delivery. Her complaints were much aggravated for two or three months previous to delivery; she had become greatly emaciated, and weakened to such an extent, that it had not been expected that she would long survive her confinement, if indeed she reached that period. Her labor was easy enough; she flowed a good deal, seemed exceedingly prostrated, had ringing in the ears, and other symptoms of exhaustion; the pulse was quick and small. On the second and third day there was some tenderness and tumefaction of the abdomen, which increased somewhat on the fourth and fifth. He had cases in midwifery before and after this, which presented nothing peculiar."

It is also mentioned in the same letter, that another physician had a case which happened last summer and another last fall, both of which recovered.

Another gentleman reports a case last December, a second case five weeks and another three weeks since. All these recovered. A case also occurred very recently in the practice of a physician in the village where the eighth patient of Dr. C. resides, which proved fatal. "This patient had some patches of erysipelas on the legs and arms. The same physician has delivered three cases since, which have all done well. There have been no other cases in this town or its vicinity recently. There have been some few cases of erysipelas." It deserves notice that the partner of Dr. C., who attended the autopsy of the man above-mentioned and took an active part in it; who also suffered very slightly from a prick under the thumb nail received during the examination, had twelve cases of midwifery between March 26th and April 12th, all of which did well, and presented no peculiar symptoms. It should also be stated, that during these 17 days he was in attendance on all the cases of erysipelas in the house where the autopsy had been performed.

I owe these facts to the prompt kindness of a gentleman whose intelligence and character are sufficient guaranty for their accuracy.

The two following letters were addressed to my friend Dr. Storer, by the gentlemen in whose practice the cases of puerperal fever occurred. His name renders it unnecessary to refer more particularly to these gentlemen, who on their part have manifested the most perfect freedom and courtesy in affording these accounts of their painful experience.

JAN. 28, 1843.

II. . . . "The time to which you allude was in 1830. The first case was in February, during a very cold time. She was confined the 4th and died the 12th. Between the 10th and 28th of this month, I attended six women in labor, all of whom did well except the last, as also two who were confined March 1st and 5th. Mrs. E., confined Feb. 28th, sickened, and died March 8th. The next day, 9th, I inspected the body, and the night after attended a lady, Mrs. B., who sickened, and died 16th. The 10th, I attended

another, Mrs. G., who sickened, but recovered. March 16th, I went from Mrs. G.'s room to attend a Mrs. H., who sickened, and died 21st. The 17th, I inspected Mrs. B. On 19th, I went directly from Mrs. H.'s room to attend another lady, Mrs. G., who also sickened, and died 22d. While Mrs. B. was sick, on 15th, I went directly from her room a few rods, and attended another woman, who was not sick. Up to 20th of this month I wore the same clothes. I now refused to attend any labor, and did not till April 21st, when having thoroughly cleansed myself, I resumed my practice, and had no more puerperal fever.

"The cases were not confined to a narrow space. The two nearest were half a mile from each other, and half that distance from my residence. The others were from two to three miles apart, and nearly that distance from my residence. There were no other cases in their immediate vicinity which came to my knowledge. The general health of all the women, was pretty good, and all the labors as good as common except the first. This woman, in consequence of my not arriving in season, and the child being half born some time before I arrived, was very much exposed to the cold at the time of confinement, and afterwards, being confined in a very open cold room. Of the six cases you perceive only one recovered.

"In the winter of 1817 two of my patients had puerperal fever, one very badly, the other not so badly. Both recovered. One other had swelled leg, or phlegmasia dolens, and one or two others did not recover as well as usual.

"In the summer of 1835 another disastrous period occurred in my practice. July 1st, I attended a lady in labor, who was afterwards quite ill and feverish; but at the time I did not consider her case a decided puerperal fever. On 8th, I attended one who did well. On 12th, one who was seriously sick. This was also an equivocal case, apparently arising from constipation and irritation of the rectum. These women were ten miles apart and five from my residence. On 15th and 20th, two who did well. On 25th, I attended another. This was a severe labor, and followed by unequivocal puerperal fever, or peritonitis. She recovered. August 2d and 3d, in about twenty-four hours I attended four

persons. Two of them did very well; one was attacked with some of the common symptoms, which however subsided in a day or two, and the other had decided puerperal fever, but recovered. This woman resided five miles from me. Up to this time I wore the same coat. All my other clothes had frequently been changed. On 6th, I attended two women, one of whom was not sick at all; but the other, Mrs. L., was afterwards taken ill. On 10th, I attended a lady, who did very well. I had previously changed all my clothes, and had no garment on which had been in a puerperal room. On 12th, I was called to Mrs. S., in labor. While she was ill, I left her to visit Mrs. L., one of the ladies who was confined on 6th. Mrs. L. had been more unwell than usual, but I had not considered her case anything more than common till this visit. I had on a surtout at this visit, which on my return to Mrs. S., I left in another room. Mrs. S. was delivered on 13th with forceps. These women both died of decided puerperal fever.

"While I attended these women in their fevers, I changed my clothes, and washed my hands in a solution of chloride of lime after each visit. I attended seven women in labor during this period, all of whom recovered without sickness.

"In my practice I have had several single cases of puerperal fever, some of whom have died and some have recovered. Until the year 1830, I had no suspicion that the disease could be communicated from one patient to another by a nurse or midwife; but I now think the foregoing facts strongly favor that idea. I was so much convinced of this fact, that I adopted the plan before related.

"I believe my own health was as good as usual at each of the above periods. I have no recollection to the contrary.

"I believe I have answered all your questions. I have been more particular on some points perhaps than necessary; but I thought you could form your own opinion better than to take mine. In 1830, I wrote to Dr. Channing a more particular statement of my cases. If I have not answered your questions sufficiently, perhaps Dr. C. may have my letter to him, and you can find your answer there."\*

\* In a letter to myself, this gentleman also stated, "I do not recollect that there was any erysipelas or any other disease particularly prevalent at the time."



BOSTON, FEB. 3, 1843.

III. "MY DEAR SIR,—I received a note from you last evening, requesting me to answer certain questions therein proposed, touching the cases of puerperal fever which came under my observation the past summer. It gives me pleasure to comply with your request, so far as it is in my power so to do, but owing to the hurry in preparing for a journey, the notes of the cases I had then taken, were lost or mislaid. The principal *facts*, however, are too vivid upon my recollection to be soon forgotten. I think, therefore, that I shall be able to give you all the information you may require.

"All the cases that occurred in my practice, took place between the 7th of May and the 17th of June, 1842.

"They were not confined to any particular part of the city. The two first cases were patients residing at the south-end, the next was at the extreme north-end, one living in Sea street and the other in Roxbury. The following is the order in which they occurred.

"Case 1. Mrs. — was confined on the 7th of May, at 5 o'clock, P.M., after a natural labor of six hours. At 12 o'clock at night, on the 9th (thirty-one hours after confinement), she was taken with severe chill, previous to which she was as comfortable as women usually are under the circumstances. She died on the 10th.

"Case 2. Mrs. — was confined on the 10th of June (four weeks after Mrs. C.), at 11, A. M., after a natural, but somewhat severe labor of 5 hours. At 7 o'clock, on the morning of the 11th, she had a chill. Died on the 12th.

"Case 3. Mrs. —, confined on the 14th of June, was comfortable until the 18th, when symptoms of puerperal fever were manifest. She died on the 20th.

"Case 4. Mrs. —, confined June 17th, at 5 o'clock, A. M., was doing well until the morning of the 19th. She died on the evening of the 21st.

"Case 5. Mrs. — was confined with her *fifth* child on the 17th of June, at 6 o'clock in the evening. This patient had been attacked with puerperal fever, at three of her previous confine-

ments, but the disease yielded to depletion and other remedies without difficulty. This time, I regret to say, I was not so fortunate. She was not attacked, as were the other patients, with a chill, but complained of extreme pain in abdomen, and tenderness on pressure, almost from the moment of her confinement. In this, as in the other cases, the disease resisted all remedies, and she died in great distress on the 22d of the same month. Owing to the extreme heat of the season, and my own indisposition, none of the subjects were examined after death. Dr. Channing, who was in attendance with me on the three last cases, proposed to have a post-mortem examination of the subject of case No. 5, but from some cause which I do not now recollect, it was not obtained.

"You wish to know whether I wore the same clothes when attending the different cases. I cannot positively say, but I should think I did not, as the weather became warmer after the first two cases; I therefore think it probable that I made a change of at least a *part* of my dress. I have had no other case of puerperal fever in my own practice for three years, save those above related, and I do not remember to have lost a patient before with this disease. While absent, last July, I visited two patients sick with puerperal fever, with a friend of mine in the country. Both of them recovered.

"The cases that I have recorded, were not confined to any particular constitution or temperament, but it seized upon the strong and the weak, the old and the young—one being over 40 years, and youngest under 18 years of age.\*\*\*\*\* If the disease is of an erysipelatous nature, as many suppose, contagionists may perhaps find some ground for their belief in the fact that for two weeks previous to my first case of puerperal fever, I had been attending a severe case of erysipelas, and the infection may have been conveyed through me to the patient; but on the otherhand, why is not this the case with other physicians, or with the same physician at all times, for since my return from the country I have had a more inveterate case of erysipelas than ever before, and no difficulty whatever has attended any of my midwifery cases."

I am assured, on unquestionable authority, that "About three years since, a gentleman in extensive midwifery business, in a neighboring State, lost in the course of a few weeks eight patients in child-bed, seven of them being undoubted cases of puerperal fever. No other physician of the town lost a single patient of this disease during the same period." And from what I have heard in conversation with some of our most experienced practitioners, I am inclined to think many cases of the kind might be brought to light by extensive inquiry.

This long catalogue of melancholy histories assumes a still darker aspect when we remember how kindly nature deals with the parturient female, when she is not immersed in the virulent atmosphere of an impure lying-in hospital, or poisoned in her chamber by the unsuspected breath of contagion. From all causes together, not more than four deaths in a thousand births and miscarriages, happened in England and Wales during the period embraced by the first Report of the Registrar-General.\* In the second Report the mortality was shown to be about five in one thousand.† In the Dublin Lying-in Hospital, during the seven years of Dr. Collins's mastership, there was one case of puerperal fever to 178 deliveries, or less than six to the thousand, and one death from this disease in 278 cases, or between three and four to the thousand.‡ Yet during this period the disease was endemic in the hospital, and might have gone on to rival the horrors of the pestilence of the Maternité, had not the poison been destroyed by a thorough purification.

In private practice, leaving out of view the cases that are to be ascribed to the self-acting system of propagation, it would seem that the disease must be far from common. Mr. White, of Manchester, says, "Out of the whole number of lying-in patients whom I have delivered (and I may safely call it a great one), I have never lost one, nor to the best of my recollection has one been greatly endangered, by the puerperal, miliary, low nervous,

\* 1st Report, p. 105.

† 2d Report, p. 73.

‡ Collin's Midwifery, p. 228, etc.

putrid malignant, or milk fever.”\* Dr. Joseph Clarke informed Dr. Collins, that in the course of *forty-five* years’ most extensive practice, he lost but *four* patients from this disease.† One of the most eminent practitioners of Glasgow, who has been engaged in very extensive practice for upwards of a quarter of a century, testifies that he never saw more than twelve cases of real puerperal fever.‡

I have myself been told by two gentlemen practising in this city, and having for many years a large midwifery business, that they had neither of them lost a patient from this disease, and by one of them that he had only seen it in consultation with other physicians. In five hundred cases of midwifery of which Dr. Storer has given an abstract in the first number of this Journal, there was only one instance of fatal puerperal peritonitis.

In the view of these facts, it does appear a singular coincidence, that one man or woman should have ten, twenty, thirty, or seventy cases of this rare disease, following their footsteps with the keenness of a beagle, through the streets and lanes of a crowded city, while the scores that cross the same paths on the same errands know it only by name. It is a series of similar coincidences that has led us to consider the dagger, the musket, and certain innocent looking white powders, as having some little claim to be regarded as dangerous. It is the practical inattention to similar coincidences that has given rise to the unpleasant but often necessary documents called *indictments*, that has sharpened a form of the cephalotome sometimes employed in the case of adults, and adjusted that modification of the fillet which delivers the world of those who happen to be too much in the way while such striking coincidences are taking place.

I shall now mention a few instances in which the disease appears to have been conveyed by the process of direct inoculation.

Dr. Campbell, of Edinburgh, states that in October, 1821, he assisted at the post-mortem examination of a patient who died

\* Op. cit. p. 115.

† Collin’s Treatise on Midwifery, p. 228.

‡ Lancet, May 4, 1833.

with puerperal fever. He carried the pelvic viscera in his pocket to the class room. The same evening he attended a woman in labor without previously changing his clothes; this patient died. The next morning he delivered a woman with the forceps; she died also, and of many others who were seized with the disease within a few weeks, three shared the same fate in succession.

In June, 1823, he assisted some of his pupils at the autopsy of a case of puerperal fever. He was unable to wash his hands with proper care, for want of the necessary accommodations. On getting home he found two patients required his assistance. He went without further ablution, or changing his clothes; both these patients died with puerperal fever.\* This same Dr. Campbell is one of Dr. Churchill's authorities against contagion.

Mr. Robertson says that in one instance within his knowledge, a practitioner passed the catheter for a patient with puerperal fever late in the evening; the same night he attended a lady who had the symptoms of the disease on the second day. In another instance a surgeon was called while in the act of inspecting the body of a woman who had died of this fever, to attend a labor; within forty-eight hours this patient was seized with the fever.†

On the 16th of March, 1831, a medical practitioner examined the body of a woman who had died a few days after delivery, from puerperal peritonitis. On the evening of the 17th he delivered a patient who was seized with puerperal fever on the 19th, and died on the 24th. Between this period and the 6th of April, the same practitioner attended two other patients, both of whom were attacked with the same disease and died.‡

In the autumn of 1829, a physician was present at the examination of a case of puerperal fever, dissected out the organs, and assisted in sewing up the body. He had scarcely reached home when he was summoned to attend a young lady in labor. In sixteen hours she was attacked with the symptoms of puerperal fever, and narrowly escaped with her life.§

\* London Med. Gaz. Dec. 10th, 1831.<sup>1</sup>

† Ibid. for Jan. 1832.

‡ London Cyc. of Pract. Med., Art. Fever, Puerperal.

§ Ibid.

In December, 1830, a midwife who had attended two fatal cases of puerperal fever at the British Lying-in Hospital, examined a patient who had just been admitted, to ascertain if labor had commenced. This patient remained two days in the expectation that labor would come on, when she returned home and was then suddenly taken in labor, and delivered before she could set out for the hospital. She went on favorably for two days, and was then taken with puerperal fever and died in thirty-six hours.\*

"A young practitioner, contrary to advice, examined the body of a patient who had died from puerperal fever; there was no epidemic at the the time; the case appeared to be purely sporadic. He delivered three other women shortly afterwards; they all died with puerperal fever, the symptoms of which broke out very soon after labor. The patients of his colleague did well, except one, where he assisted to remove some coagula from the uterus; she was attacked in the same manner as those whom he had attended, and died also." The writer in the British and Foreign Medical Review, from whom I quote this statement—and who is no other than Dr. Rigby—adds, "we trust that this fact alone will forever silence such doubts, and stamp the well-merited epithet of 'criminal,' as above quoted, upon such attempts."†

From the cases given by Mr. Ingleby, I select the following. Two gentlemen, after having been engaged in conducting the post-mortem examination of a case of puerperal fever, went in the same dress, each respectively, to a case of midwifery. "The one patient was seized with the rigor about thirty hours afterwards. The other patient was seized with a rigor the third morning after delivery. *One recovered, one died.*"‡ One of these same gentlemen attended another woman in the same clothes two days after the autopsy referred to. "The rigor did not take place until the evening of the fifth day from the first visit. *Result fatal.*" These cases belonged to a series of seven, the first of which was thought to have originated in a case of erysipelas. "Several cases of a mild character followed the foregoing seven, and their nature

\* Ibid.

† Brit. and For. Medical Review, for Jan. 1842, p. 112.

‡ Edin. Med. and Surg. Journal, April, 1838.

being now most unequivocal, my friend declined visiting all midwifery cases for a time; and there was no recurrence of the disease." These cases occurred in 1833. Five of them proved fatal. Mr. Ingleby gives another series of seven cases which occurred to a practitioner in 1836, the first of which was also attributed to his having opened several erysipelatous abscesses a short time previously.

I need not refer to the case lately read before this Society, in which a physician went, soon after performing an autopsy of a case of puerperal fever, to a woman in labor, who was seized with the same disease and perished. The forfeit of that error has been already paid.

At the meeting of the Medical and Chirurgical Society before referred to, Dr. Merriman related an instance occurring in his own practice, which excites a reasonable suspicion that two lives were sacrificed to a still less dangerous experiment. He was at the examination of a case of puerperal fever at 2 o'clock in the afternoon. *He took care not to touch the body.* At 9 o'clock the same evening he attended a woman in labor; she was so nearly delivered that he had scarcely any thing to do. The next morning she had severe rigors, and in 48 hours was a corpse. Her infant had erysipelas and died in two days.\*

In connection with the facts which have been stated, it seems proper to allude to the dangerous and often fatal effects which have followed from wounds received in the post-mortem examination of patients who have died of puerperal fever. The fact that such wounds are attended with peculiar risk has been long noticed. I find that Chaussier was in the habit of cautioning his students against the danger to which they were exposed in these dissections.† The head *pharmacien* of the Hotel Dieu, in his analysis of the fluid effused in puerperal peritonitis, says that practitioners are convinced of its deleterious qualities, and that it is very dangerous to apply it to the denuded skin.‡ Sir Benjamin Brodie speaks of it as being well known that the inoculation of

\* Lancet, May 2d, 1840.

† Stein, l'Art de Accoucher, 1794. Dict. des Sciences Medicales, Art. Puerperal.

‡ Journal de Pharmacie, Jan. 1836.

lymph or pus from the peritoneum of a puerperal patient is often attended with dangerous and even fatal symptoms. Three cases in confirmation of this statement, two of them fatal, have been reported to this Society within a few months. Of about fifty cases of injuries of this kind, of various degrees of severity, which I have collected from different sources, at least twelve were instances of infection from puerperal peritonitis. Some of the others are so stated as to render it probable that they may have been of the same nature. Five other cases were of peritoneal inflammation; three in males. Three were of what was called enteritis, in one instance complicated with erysipelas; but it is well known that this term has been often used to signify inflammation of the peritoneum covering the intestines. On the other hand, no case of typhus or typhoid fever is mentioned as giving rise to dangerous consequences, with the exception of the single instance of an undertaker mentioned by Mr. Travers, who seems to have been poisoned by a fluid which exuded from the body. The other accidents were produced by dissection, or some other mode of contact with bodies of patients who had died of various affections. They also differed much in severity, the cases of puerperal origin being among the most formidable and fatal. Now a moment's reflection will show that the number of cases of serious consequences ensuing from the dissection of the bodies of those who have perished of puerperal fever, is so vastly disproportioned to the relatively small number of autopsies made in this complaint as compared with typhus, or pneumonia, (from which last disease not one case of poisoning happened), and still more from all diseases put together, that the conclusion is irresistible that a most fearful morbid poison is often generated in the course of this disease. Whether or not it is *sui generis*, confined to this disease, or produced in some others, as for instance erysipelas, I need not stop to inquire.

In connection with this may be taken the following statement of Dr. Rigby. "That the discharges from a patient under puerperal fever are in the highest degree contagious, we have abundant evidence in the history of lying-in hospitals. The puerperal abscesses are also contagious, and may be communicated to



healthy lying-in women by washing with the same sponge; this fact has been repeatedly proved in the Vienna Hospital; but they are equally communicable to women not pregnant; on more than one occasion the women engaged in washing the soiled bed-linen of the General Lying-in Hospital have been attacked with abscess in the fingers or hands, attended with rapidly spreading inflammation of the cellular tissue.”\*

Now add to all this the undisputed fact that within the walls of lying-in hospitals there is often generated a miasm, palpable as the chlorine used to destroy it, tenacious so as in some cases almost to defy extirpation, deadly in some institutions as the plague; which has killed women in a private hospital of London so fast that they were buried two in one coffin to conceal its horrors; which enabled Tonellé to record two hundred and twenty-two autopsies at the Maternité of Paris; which has led Dr. Lee to express his deliberate conviction that the loss of life occasioned by these institutions completely defeats the object of their founders; and out of this train of cumulative evidence, the multiplied groups of cases clustering about individuals, the deadly results of autopsies, the inoculation by fluids from the living patient, the murderous poison of hospitals, does there not result a conclusion that laughs all sophistry to scorn, and renders all argument an insult?

I have had occasion to mention some instances in which there was an apparent relation between puerperal fever and erysipelas. The length to which this paper has extended does not allow me to enter into the consideration of this most important subject. I will only say that the evidence appears to me altogether satisfactory that some most fatal series of puerperal fever have been produced by an infection originating in the matter or effluvia of erysipelas. In evidence of some connection between the two diseases, I need not go back to the older authors, as Pouteau or Gordon, but will content myself with giving the following references, with their dates; from which it will be seen that the testimony has been constantly coming before the profession for the last few years.

\* *System of Midwifery*, p. 292.

London Cyclopaedia of Practical Medicine—article Puerperal Fever. 1833.

Mr. Ceeley's Account of the Puerperal Fever at Aylesbury. Lancet, 1835.

Dr. Ramsbotham's Lecture. London Medical Gazette, 1835.

Mr. Yates Ackerley's Letter in the same Journal, 1838.

Mr. Ingleby on Epidemic Puerperal Fever. Edinburgh Medical and Surgical Journal, 1838.

Mr. Paley's Letter. London Medical Gazette, 1839.

Remarks at the Medical and Chirurgical Society. Lancet, 1840.

Dr. Rigby's System of Midwifery. 1841.

Nunneley on Erysipelas—a work which contains a large number of references on the subject. 1841.

British and Foreign Quarterly Review, 1842.

Dr. S. Jackson, of Northumberland, as already quoted from the Summary of the College of Physicians, 1842.

And lastly, a startling series of cases by Mr. Storrs, of Doncaster, to be found in the American Journal of the Medical Sciences for January, 1843.

The relation of puerperal fever with other continued fevers, would seem to be remote and rarely obvious. Hey refers to two cases of synochus occurring in the Royal Infirmary of Edinburgh, in women who had attended upon puerperal patients. Dr. Collins refers to several instances in which puerperal fever has appeared to originate from a continued proximity to patients suffering with typhus.\*

Such occurrences as those just mentioned, though most important to be remembered and guarded against, hardly attract our notice in the midst of the gloomy facts by which they are surrounded. Of these facts, at the risk of fatiguing repetitions, I have summoned a sufficient number, as I believe, to convince the most incredulous, that every attempt to disguise the truth which underlies them all, is useless.

It is true that some of the historians of the disease, especially

\* Treatise on Midwifery, p. 228.

Hulme, Hull and Leake, in England; Tonellé, Dugès and Baudelocque, in France, profess not to have found puerperal fever contagious. At the most they give us mere negative facts, worthless against an extent of evidence which now overlaps the widest range of doubt, and doubles upon itself in the redundancy of superfluous demonstration. Examined in detail, this and much of the show of testimony brought up to stare the daylight of conviction out of countenance, proves to be in a great measure unmeaning or inapplicable, as might be easily shown were it necessary. Nor do I feel the necessity of enforcing the conclusion which arises spontaneously from the facts which have been enumerated, by formally citing the opinions of those grave authorities who have for the last half century been sounding the unwelcome truth it has cost so many lives to establish.

"It is to the British practitioner," says Dr. Rigby, "that we are indebted for strongly insisting upon this important and dangerous character of puerperal fever."\*

The names of Gordon, John Clarke, Denman, Burns, Young,† Hamilton,‡ Haighton,§ Good,|| Waller,¶ Blundell, Gooch, Ramsbotham, Douglas,\*\* Lee, Ingleby, Locock,†† Abercrombie,‡‡ Alison,§§ Travers,||| Rigby, and Watson,¶¶ many of whose writings I have already referred to, may have some influence with those who prefer the weight of authorities to the simple deductions of their own reason from the facts laid before them. A few continental writers have adopted similar conclusions.\*\*\* It gives me

\* British and Foreign Med. Review for Jan. 1842.

† Encyc. Britannica, xiii, 467, Art. Medicine.

‡ Outlines of Midwifery, p. 109.

§ Oral Lectures, &c.

|| Study of Medicine, ii. 195.

¶ Medical and Physical Journal, July, 1830.

\*\* Dublin Hosp. Reports for 1822.

†† Library of Pract. Medicine, i. 373.

‡‡ Researches on Diseases of the Stomach, &c. p. 181.

§§ Lib. of Pract. Medicine, Vol. i. p. 96.

||| Further Researches on Constitutional Irritation, p. 128.

¶¶ Lond. Med. Gaz. Feb. 1842.

\*\*\* See British and Foreign Medical Review, Vol. iii. p. 525, and Vol. iv. p. 517. Also Ed. Med. and Surg. Journal for July, 1824, and American Journal of Med. Sciences for Jan. 1841.

pleasure to remember that while the doctrine has been unceremoniously discredited in one of the leading Journals,\* and made very light of by teachers in two of the principal Medical Schools of this country, Dr. Channing has for many years inculcated and enforced by examples the danger to be apprehended and the precautions to be taken in the disease under consideration.

I have no wish to express any harsh feeling with regard to the painful subject that has come before us. If there are any so far excited by the story of these dreadful events, that they ask for some word of indignant remonstrance, to show that science does not turn the hearts of its followers into ice or stone, let me remind them that such words have been uttered by those who speak with an authority I could not claim.† It is as a lesson rather than as a reproach that I call up the memory of these irreparable errors and wrongs. No tongue can tell the heart-breaking calamity they have caused; they have closed the eyes just opened upon a new world of love and happiness; they have bowed the strength of manhood into the dust; they have cast the helplessness of infancy into the stranger's arms, or bequeathed it with less cruelty the death of its dying parent. There is no tone deep enough for regret, and no voice loud enough for warning. The woman about to become a mother, or with her new-born infant upon her bosom, should be the object of trembling care and sympathy wherever she bears her tender burden, or stretches her aching limbs. The very outcast of the streets has pity upon her sister in degradation when the seal of promised maternity is impressed upon her. The remorseless vengeance of the law, brought down upon its victim by a machinery as sure as destiny, is arrested in its fall at a word which reveals her transient claim for mercy. The solemn prayer of the liturgy singles out her sorrows from the multiplied trials of life, to plead for her in the hour of peril. God forbid that any member of the profession to which she trusts her life, doubly precious at that eventful period, should hazard it negligently, unadvisedly, or selfishly!

\* Phil. Med. Journ. Vol. xii. p. 364.

† Dr. Blundell and Dr. Rigby in the works already cited.

There may be some among those whom I address, who are disposed to ask the question, What course are we to follow in relation to this matter? The facts are before them, and the answer must be left to their own judgment and conscience. If any should care to know my own conclusions, they are the following; and in taking the liberty to state them very freely and broadly, I would ask the inquirer to examine them as freely in the light of the evidence which has been laid before him.

1. A physician holding himself in readiness to attend cases of midwifery, should never take any active part in the post-mortem examination of cases of puerperal fever.

2. If a physician is present at such autopsies, he should use thorough ablution, change every article of dress, and allow twenty-four hours or more to elapse before attending to any case of midwifery. It may be well to extend the same caution to cases of simple peritonitis.

3. Similar precautions should be taken after the autopsy or surgical treatment of cases of erysipelas, if the physician is obliged to unite such offices with his obstetrical duties, which is in the highest degree inexpedient.

4. On the occurrence of a single case of puerperal fever in his practice, the physician is bound to consider the next female he attends in labor, unless some weeks, at least, have elapsed, as in danger of being infected by him, and it is his duty to take every precaution to diminish her risk of disease and death.

5. If within a short period two cases of puerperal fever happen close to each other, in the practice of the same physician, the disease not existing or prevailing in the neighborhood, he would do wisely to relinquish his obstetrical practice for at least one month, and endeavor to free himself by every available means from any noxious influence he may carry about with him.

6. The occurrence of three or more closely connected cases, in the practice of one individual, no others existing in the neighborhood, and no other sufficient cause being alleged for the coincidence, is *prima facie* evidence that he is the vehicle of contagion.

7. It is the duty of the physician to take every precaution that the disease shall not be introduced by nurses or other assistants,

by making proper inquiries concerning them, and giving timely warning of every suspected source of danger.

8. Whatever indulgence may be granted to those who have heretofore been the ignorant causes of so much misery, the time has come when the existence of a *private pestilence* in the sphere of a single physician should be looked upon not as a misfortune but a crime; and in the knowledge of such occurrences, the duties of the practitioner to his profession, should give way to his paramount obligations to society.



# PUERPERAL FEVER,

AS A

## PRIVATE PESTILENCE.

BY

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*H. H. 177*

BOSTON:

TICKNOR AND FIELDS.

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# THE POINT AT ISSUE.

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## THE AFFIRMATIVE.

The disease known as Puerperal Fever is so far contagious, as to be frequently carried from patient to patient by physicians and nurses.' — *O. W. Holmes, 1843.*

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## THE NEGATIVE.

'The result of the whole discussion, will, I trust, serve, not only to exalt your views of the value and dignity of our profession, but to divest your minds of the overpowering dread that you can ever become, especially to woman, under the extremely interesting circumstances of gestation and parturition, the minister of evil; that you can ever convey, in any possible manner, a horrible virus, so destructive in its effects, and so mysterious in its operations as that attributed to puerperal fever.' — *Professor Hodge, 1852.*

'I prefer to attribute them to accident, or Providence, of which I can form a conception, rather than to a contagion of which I cannot form any clear idea, at least as to this particular malady.' — *Professor Meigs, 1852.*

.... 'In the propagation of which they have no more to do, than with the propagation of cholera from Jessore to San Francisco, and from Mauritius to St. Petersburg.' — *Professor Meigs, 1854.*

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'I arrived at that certainty in the matter, that I could venture to foretell what women would be affected with the disease, upon hearing by what midwife they were to be delivered, or by what nurse they were to be attended, during their lying-in; and, almost in every instance, my prediction was verified.' — *Gordon, 1795.*

'A certain number of deaths is caused every year by the contagion of puerperal fever, communicated by the nurses and medical attendants.' — *Farr, in Fifth Annual Report of Registrar-General of England, 1843.*

.... 'boards of health, if such exist, or without them, the medical institutions of a country, should have the power of coercing, or of inflicting some kind of punishment on those who recklessly go from cases of puerperal fevers to parturient or puerperal females, without using due precaution; and who, having been shown the risk, criminally encounter it, and convey pestilence and death to the persons they are employed to aid in the most interesting and suffering period of female existence.' — *Copland's Medical Dictionary, Art. Puerperal States and Diseases. 1853.*

'We conceive it unnecessary to go into detail to prove the contagious nature of this disease, as there are few, if any, American practitioners who do not believe in this doctrine.' — *Dr. Lee, in Additions to Article last cited.*



# Puerperal Fever as a Private Pestilence

BY

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## INTRODUCTION

**I**T HAPPENED, some years ago, that a discussion arose in a Medical Society, of which I was a member, involving the subject of a certain supposed cause of disease, about which something was known, a good deal suspected, and not a little feared. The discussion was suggested by a case, reported at the preceding meeting, of a physician who made an examination of the body of a patient who had died with puerperal fever, and who himself died in less than a week, apparently in consequence of a wound received at the examination, having attended several women in confinement in the mean time, all of whom, as alleged, were attacked with puerperal fever.

Whatever apprehensions and beliefs were entertained, it was plain that a fuller knowledge of the facts relating to the subject would be acceptable to all present. I therefore felt that it would be doing a good service to look into the best records I could find, and inquire of the most trustworthy practitioners I knew, to learn what experience had to teach in the matter, and arrived at the results contained in the following pages.

The Essay was read before the Boston Society for Medical Improvement, and at the request of the Society, printed in the

New England Quarterly Journal of Medicine and Surgery, for April, 1843. As this Journal never obtained a large circulation, and ceased to be published after a year's existence, and as the few copies I had struck off separately were soon lost sight of among the friends to whom they were sent, the Essay can hardly be said to have been fully brought before the Profession.

The subject of this Paper has the same profound interest for me at the present moment, as when I was first collecting the terrible evidence out of which, as it seems to me, the commonest exercise of reason could not help shaping the truth it involved. It is not merely on account of the bearing of the question,—if there is a question,—on all that is most sacred in human life and happiness, that the subject cannot lose its interest. It is because I most fully believe that a fair statement of the facts must produce its proper influence on a very large proportion of well constituted and unprejudiced minds. Individuals may, here and there, resist the practical bearing of the evidence on their own feelings or interests; some may fail to see its meaning, as some persons may be found who cannot tell red from green; but I cannot doubt that most readers will be satisfied and convinced, to loathing, long before they have finished the dark obituary calendar laid before them.

I do not know that I shall ever again have so good an opportunity of being useful as was granted me by the raising of the question which produced this Essay. For I have abundant evidence that it has made many practitioners more cautious in their relations with puerperal females, and I have no doubt it will do so still, if it has a chance of being read, though it should call out a hundred counterblasts, proving to the satisfaction of their authors that it proved nothing. And, for my own part, I had rather rescue one mother from being poisoned by her attendant, than claim to have saved forty out of fifty patients, to whom I had carried the disease. Thus, I am willing to avail myself of any hint coming from without, to offer this paper once more to the press. The occasion has presented itself, as will be seen, in a convenient, if not in a flattering form.

I send this Essay again to the MEDICAL PROFESSION, without the change of a word or syllable. I find, on reviewing it, that it anticipates and eliminates those secondary questions which cannot be entertained for a moment, until the one great point of fact is peremptorily settled. In its very statement of the doctrine maintained, it avoids all discussion of the nature of the disease '*known as puerperal fever*;' and all the somewhat stale philology of the word *contagion*. It mentions, fairly enough, the names of sceptics, or unbelievers as to the reality of personal transmission; of Dewees, of Tonnellé, of Dugès, of Baudelocque and others; of course, not including those whose works were then unwritten or unpublished; nor enumerating all the continental writers who, in ignorance of the great mass of evidence accumulated by British practitioners, could hardly be called well informed on this subject. It meets all the array of negative cases,—those in which disease did not follow exposure,—by the striking example of small pox, which, although one of the most contagious of diseases, is subject to the most remarkable irregularities and seeming caprices in its transmission. It makes full allowance for other causes besides personal transmission, especially for epidemic influences. It allows for the possibility of different modes of conveyance of the destructive principle. It recognises and supports the belief that a series of cases may originate from a single primitive source which affects each new patient in turn; and especially from cases of Erysipelas. It does not undertake to discuss the theoretical aspect of the subject; that is a secondary matter of consideration. Where facts are numerous, and unquestionable, and unequivocal in their significance, theory must follow them as it best may, keeping time with their step, and not go before them, marching to the sound of its own drum and trumpet. Having thus narrowed its area to a limited practical platform of discussion, a matter of life and death, and not of phrases or theories, it covers every inch of it with a mass of evidence which I conceive a Committee of Husbands, who can count coincidences and draw conclusions as well as a Synod of Accoucheurs, would justly consider as affording ample reasons for an *unceremonious dismissal* of a practitioner, (if it is conceivable that such a step could be waited

for,) after five or six funerals had marked the path of his daily visits, while other practitioners were not thus escorted. To the Profession, therefore, I submit the paper in its original form, and leave it to take care of itself.

To the MEDICAL STUDENTS, into whose hands this Essay may fall, some words of introduction may be appropriate, and perhaps, to a small number of them, necessary. There are some among them who, from youth, or want of training, are easily bewildered and confused in any conflict of opinions into which their studies lead them. They are liable to lose sight of the main question in collateral issues, and to be run away with by suggestive speculations. They confound belief with evidence, often trusting the first because it is expressed with energy, and slighting the latter because it is calm and unimpassioned. They are not satisfied with proof; they cannot believe a point is settled, so long as everybody is not silenced. They have not learned that error is got out of the minds that cherish it, as the *tænia* is removed from the body, one joint, or a few joints at a time, for the most part, rarely the whole evil at once. They naturally have faith in their instructors, turning to them for truth, and taking what they may choose to give them; babes in knowledge, not yet able to tell the breast from the bottle, pumping away for the milk of truth at all that offers, were it nothing better than a Professor's shrivelled forefinger.

In the earliest and embryonic stage of professional development, any violent impression on the instructor's mind is apt to be followed by some lasting effect on that of the pupil. No mother's mark is more permanent than the mental *nævi* and moles, and excrescences, and mutilations, that students carry with them out of the lecture-room, if once the teeming intellect which nourishes theirs, has been scared from its propriety by any misshapen fantasy. Even an impatient or petulant expression, which to a philosopher would be a mere index of the low state of amiability of the speaker at the moment of its utterance, may pass into the young mind as an element of its future constitution, to injure its temper or corrupt its judgment. It is a

duty, therefore, which we owe to this younger class of students, to clear any important truth, which may have been rendered questionable in their minds by such language, or any truth-teller against whom they may have been prejudiced by hasty epithets, from the impressions such words have left. Until this is done, they are not ready for the question, where there is a question for them to decide. Even if we ourselves are the subjects of the prejudice, there seems to be no impropriety in showing that this prejudice is local or personal, and not an acknowledged conviction with the public at large. It may be necessary to break through our usual habits of reserve to do this, but this is a fault of the position in which others have placed us.

Two widely known and highly esteemed practitioners, Professors in two of the largest Medical Schools of the Union, teaching the branch of art which includes the Diseases of Women, and therefore speaking with authority; addressing in their lectures and printed publications large numbers of young men, many of them in the tenderest immaturity of knowledge, have recently taken ground in a formal way against the doctrine maintained in this paper.\* The first of the two publications, Dr. Hodge's Lecture, while its theoretical considerations and negative experiences do not seem to me to require any further notice than such as lay ready for them in my Essay written long before, is, I am pleased to say, unobjectionable in tone and language, and may be read without offence.

This can hardly be said of the chapter of Dr. Meigs's volume which treats of Contagion in Childbed Fever. There are expressions used in it which might well put a stop to all scientific discussions, were they to form the current coin in our exchange of opinions. I leave the 'very young gentlemen,' whose careful expositions of the results of practice in more than six thousand

\* On the Non-Contagious Character of Puerperal Fever: An Introductory Lecture. By Hugh L. Hodge, M.D., Professor of Obstetrics in the University of Pennsylvania. Delivered Monday, October 11, 1852. Philadelphia: 1852.

On the Nature, Signs and Treatment of Childbed Fevers: in a Series of Letters Addressed to the Students of his Class. By Charles D. Meigs, M.D., Professor of Midwifery and the Diseases of Women and Children in Jefferson Medical College, Philadelphia, etc., etc. Philadelphia: 1854. Letter VI.

cases, are characterized as 'the jejune and fizenless dreamings of sophomore writers,' to the sympathies of those 'dear young friends,' and 'dear young gentlemen,' who will judge how much to value their instructor's counsel to think for themselves, knowing what they are to expect if they happen not to think as he does.

One unpalatable expression, I suppose the laws of construction oblige me to appropriate to myself, as my reward for a certain amount of labor bestowed on the investigation of a very important question of evidence, and a statement of my own practical conclusions. I take no offence and attempt no retort. No man makes a quarrel with me over the counterpane that covers a mother, with her new-born infant at her breast! There is no epithet in the vocabulary of slight and sarcasm that can reach my personal sensibilities in such a controversy. Only just so far as a disrespectful phrase may turn the student aside from the examination of the evidence, by discrediting or dishonoring the witness, does it call for any word of notice.

I appeal from the disparaging language by which the Professor in the Jefferson School of Philadelphia would dispose of my claims to be listened to. I appeal, not to the vote of the Society for Medical Improvement, although this was an unusual evidence of interest in the paper in question, for it was a vote passed among my own townsmen; nor to the opinion of any American, for none know better than the Professors in the great Schools of Philadelphia how cheaply the praise of native contemporary criticism is obtained. I appeal to the recorded opinions of those whom I do not know, and who do not know me, nor care for me, except for the truth that I may have uttered; to Copland, in his Medical Dictionary, who has spoken of my Essay in phrases to which the pamphlets of American 'scribblers' are seldom used from European authorities; to Ramsbotham, whose compendious eulogy is all that self-love could ask; to the Fifth Annual Report of the Registrar-General of England, in which the second-hand abstract of my Essay figures largely, and not without favorable comment, in an important appended paper. These testimonies, half forgotten until this circumstance recalled them, are dragged into the light, not in a paroxysm of vanity, but to show that there

may be food for thought in the small pamphlet which the Philadelphia Teacher treats so lightly. They were at least unsought for, and would never have been proclaimed but for the sake of securing the privilege of a decent and unprejudiced hearing.

I will take it for granted that they have so far counterpoised the depreciating language of my fellow-countryman and fellow-teacher, as to gain me a reader here and there among the youthful class of students I am now addressing. It is only for their sake that I think it necessary to analyze, or explain, or illustrate, or corroborate any portion of the following Essay. But I know that nothing can be made too plain for beginners, and as I do not expect the practitioner, or even the more mature student, to take the trouble to follow me through an Introduction which I consider wholly unnecessary and superfluous for them, I shall not hesitate to stoop to the most elementary simplicity for the benefit of the younger student. I do this more willingly, because it affords a good opportunity, as it seems to me, of exercising the untrained mind in that medical logic which does not seem to have been either taught or practised in our schools of late, to the extent that might be desired.

I will now exhibit, in a series of propositions reduced to their simplest expression, the same essential statements and conclusions as are contained in the Essay, with such commentaries and explanations as may be profitable to the inexperienced class of readers addressed.

I. It has been long believed by many competent observers, that Puerperal Fever (so called) is sometimes carried from patient to patient by medical assistants.

II. The express object of this Essay is to prove that it is so carried.

III. In order to prove this point, it is not necessary to consult any medical theorist, as to whether or not it is consistent with his preconceived notions that such a mode of transfer should exist.

IV. If the medical theorist insists on being consulted, and we see fit to indulge him, he cannot be allowed to assume that the alleged laws of contagion, *deduced from observation* in other dis-



eases, shall be cited to disprove the alleged laws *deduced from observation* in this. Science would never make progress under such conditions. Neither the long incubation of hydrophobia, nor the protecting power of vaccination, would ever have been admitted, if the results of observation in these affections had been rejected as contradictory to the previously ascertained laws of contagion.

V. The disease in question is not a common one; producing, on the average, about three deaths in a thousand births, according to the English Registration returns which I have examined.

VI. When an unusually large number of cases of this disease occur about the same time, it is inferred, therefore, that there exists some special cause for this increased frequency. If the disease prevails extensively over a wide region of country, it is attributed without dispute to an *epidemic* influence. If it prevails in a single locality, as in a hospital, and not elsewhere, this is considered proof that some *local* cause is there active in its production.

VII. When a large number of cases of this disease occur in rapid succession, in one individual's ordinary practice, and few or none elsewhere, these cases appearing in scattered localities, in patients of the same average condition as those who escape under the care of others; there is the same reason for connecting the cause of the disease with the *person* in this instance, as with the *place* in that last mentioned.

VIII. Many series of cases, answering to these conditions, are given in this Essay, and many others will be referred to which have occurred since it was written.

IX. The alleged results of observation may be *set aside*; first, because the so-called facts are in their own nature equivocal; secondly, because they stand on insufficient authority; thirdly, because they are not sufficiently numerous. But, in this case, the disease is one of striking and well marked character; the witnesses are experts, interested in denying and disbelieving the facts; the number of consecutive cases in many instances frightful, and the number of series of cases such, that I have no room for many of them except by mere reference.

X. These results of observation, being admitted, may, we will suppose, be *interpreted* in different methods. Thus the coincidences may be considered the effect of *chance*. I have had the chances calculated by a competent person, that a given practitioner, A., shall have sixteen fatal cases in a month, on the following data: A. to average attendance upon two hundred and fifty births in a year; three deaths in one thousand births to be assumed as the average from puerperal fever; no epidemic to be at the time prevailing. It follows, from the answer given me, that if we suppose every one of the five hundred thousand annual births of England to have been recorded during the last half century, there would not be one chance in a million million million millions, that one such series should be noted. No possible fractional error in this calculation can render the chance a working probability. Applied to dozens of series of various lengths, it is obviously an absurdity. Chance, therefore, is out of the question as an explanation of the admitted coincidences.

XI. There is, therefore, *some* relation of cause and effect, between the physician's presence and the patient's disease.

XII. Until it is proved to what *removable condition* attaching to the attendant the disease is owing, he is bound to stay away from his patients so soon as he finds himself singled out to be tracked by the disease. How long, and with what other precautions, I have suggested, without dictating, at the close of my essay. If the physician does not at once act on any reasonable suspicion of his being the medium of transfer, the families where he is engaged, if they are allowed to know the facts, should decline his services for the time. His feelings on the occasion, however interesting to himself, should not be even named in this connection. A physician who talks about *ceremony* and *gratitude*, and *services rendered*, and the *treatment he got*, surely forgets himself; it is impossible that he should seriously think of these small matters where there is even a question whether he may not carry disease, and death, and bereavement into any one of 'his families,' as they are sometimes called.

I will now point out to the young student the mode in which he may relieve his mind of any confusion, or possibly, if *very* young,

any doubt, which the perusal of Dr. Meigs's Sixth Letter may have raised in his mind.

The most prominent ideas of the Letter are, first, that the transmissible nature of puerperal fever appears improbable, and, secondly, that it would be very inconvenient, to the writer. Dr. Woodville, Physician to the Small Pox and Inoculation Hospital in London, found it improbable, and exceedingly inconvenient to himself, that cow-pox should prevent small-pox; but Dr. Jenner took the liberty to prove the fact, notwithstanding.

I will first call the young student's attention to the show of negative facts, (exposure without subsequent disease), of which much seems to be thought. And I may, at the same time, refer him to Dr. Hodge's Lecture, where he will find the same kind of facts and reasoning. Let him now take up Watson's Lectures, the good sense and spirit of which have made his book a universal favorite, and open to the chapter on Continued Fever. He will find a paragraph containing the following sentence: 'A man might say, "I was in the battle of Waterloo, and saw many men around me fall down and die, and it was said that they were struck down by musket balls; but I know better than that, for I was there all the time, and so were many of my friends, and we were never hit by any musket balls. Musket balls, therefore, could not have been the cause of the deaths we witnessed." And if, like contagion, they were not palpable to the senses, such a person might go on to affirm that no proof existed of there being any such thing as musket balls.' Now let the student turn back to the Chapter on Hydrophobia in the same volume. He will find that John Hunter knew a case in which, of twenty-one persons bitten, only one died of the disease. He will find that one dog at Charenton was bitten at different times by thirty different mad dogs, and outlived it all. Is there no such thing, then, as hydrophobia? Would one take no especial precautions if his wife, about to become a mother, had been bitten by a rabid animal, because so many escape? Or let him look at Underwood on Diseases of Children,\* and he will find the case of a young woman who was inoculated eight times in thirty days, at the same time attending

\* Philadelphia, 1842, p. 244, note.

several children with small pox, and yet was not infected. But seven weeks afterwards she took the disease and died.

It would seem as if the force of this argument could hardly fail to be seen, if it were granted that every one of these series of cases were so reported as to prove that there could have been no transfer of disease. *There is not one of them* so reported, in the Lecture or the Letter, as to prove that the disease may not have been carried by the practitioner. I strongly suspect that it was so carried in some of these cases, but from the character of the very imperfect evidence, the question can never be settled without further disclosures.

Although the Letter is, as I have implied, principally taken up with secondary and collateral questions, and might therefore be set aside as in the main irrelevant, I am willing, for the student's sake, to touch some of these questions briefly, as an illustration of its logical character.

The first thing to be done, as I thought when I wrote my Essay, was to throw out all discussions of the word *contagion*, and this I did effectually by the careful wording of my statement of the subject to be discussed. My object was not to settle the etymology or definition of a word, but to show that women had often died in childbed, poisoned in some way by their medical attendants. On the other point, I, at least, have no controversy with any body, and I think the student will do well to avoid it in this connection. If I must define my position, however, as well as the term in question, I am contented with Worcester's definition; provided always this avowal do not open another side-controversy on the merits of his Dictionary, which Dr. Meigs has not cited, as compared with Webster's, which he has.

I cannot see the propriety of insisting that all the laws of the eruptive fevers must necessarily hold true of this peculiar disease of puerperal women. If there were any such propriety, the laws of the eruptive fevers must at least be stated correctly. It is not true for instance, as Dr. Meigs states, that contagion is 'no respecter of persons;' that 'it attacks all individuals alike.' To give one example: Dr. Gregory, of the Small Pox Hospital, who ought to know, says that persons pass through life apparently insensible

to or unsusceptible of the small-pox virus, and that the same persons do not take the vacciné disease.

As to the short time of incubation, of which so much is made, we have no right to decide beforehand whether it shall be long or short, in the cases we are considering. A dissection wound may produce symptoms of poisoning in six hours; the bite of a rabid animal may take as many months.

After the student has read the case in Dr. Meig's 136th paragraph, and the following one, in which he exclaims against the idea of contagion, because the patient, delivered on the 26th of December, was attacked in twenty-four hours, and died on the third day, let him read what happened at the 'Black Assizes' of 1577 and 1750. In the first case, six hundred persons sickened the same night of the exposure, and three hundred more in three days.\* Of those attacked in the latter year, the exposure being on the 11th of May, Alderman Lambert died on the 13th, Under-Sheriff Cox on the 14th, and many of note before the 20th.† But these are old stories. Let the student listen then to Dr. Gerhard, whose reputation as a cautious observer, he may be supposed to know. 'The nurse was shaving a man, who died in a few hours after his entrance; he inhaled his breath, which had a nauseous taste, and in an hour afterwards was taken with nausea, cephalalgia, and singing of the ears. From that *moment* the attack began, and assumed a severe character. The assistant was supporting another patient, who died soon afterwards; he felt the pungent heat upon his skin, and was taken immediately with the symptoms of typhus.'‡ It is by notes of cases, rather than notes of admiration, that we must be guided, when we study the Revised Statutes of Nature, as laid down from the curule chairs of Medicine.

Let the student read Dr. Meigs's 140th paragraph soberly, and then remember that not only does he *infer*, *suspect* and *surmise*, but he actually *asserts* (page 154), 'there was poison in the house,' because three, out of five patients admitted into a ward, had

\* Elliotson's Practice, p. 299.

† Rees's Cyc. Art. Contagion.

‡ Am. Journ. Med. Sciences, Feb. 1837, p. 299.

puerperal fever, and died. Have I not as much right to draw a positive inference from 'Dr. A's' seventy exclusive cases, as he from the three cases in the ward of the Dublin Hospital? All practical medicine, and all action in common affairs, is founded on inferences. How does Dr. Meigs know that the patients he bled in puerperal fever would not have all got well if he had not bled them?

'You see a man discharge a gun at another; you see the flash, you hear the report, you see the person fall a lifeless corpse; and you *infer*, from all these circumstances, that there was a ball discharged from the gun, which entered his body and caused his death, because such is the usual and natural cause of such an effect. But you did not see the ball leave the gun, pass through the air, and enter the body of the slain; and your testimony to the fact of killing is, therefore, only inferential,—in other words, circumstantial. It is *possible* that no ball was in the gun; and we *infer* that there was, only because we cannot account for death on any other supposition.'\*

'The question always comes to this,—Is the circumstance of intercourse with the sick followed by the appearance of the disease in a proportion of cases so much greater than any other circumstance common to any portion of the inhabitants of the place under observation, as to make it inconceivable that the succession of cases occurring in persons having that intercourse should have been the result of chance? If so, the inference is unavoidable, that that intercourse must have acted as a cause of the disease. *All observations which do not bear strictly on that point are irrelevant*, and, in the case of an epidemic first appearing in a town or district, a succession of *two cases* is sometimes sufficient to furnish evidence, which, on the principle I have stated, is nearly irresistible.'†

Possibly an inexperienced youth may be awe-struck by the quotation from Cuvier. These words, or their equivalent, are certainly to be found in his Introduction. So are the words 'top not come down'! to be found in the Bible, and they were as much meant for the ladies' head-dresses, as the words of Cuvier were

\* Chief Justice Gibson, in Am. Law Journal, vol. vi. p. 123.

† Dr. Alison.

meant to make clinical observation wait for a permit from any body to look with its eyes and count on its fingers. Let the inquiring youth read the whole Introduction, and he will see what they mean.

I intend no breach of courtesy, but this is a proper place to warn the student against skimming the prefaces and introductions of works for mottos and embellishments to his thesis. He cannot learn anatomy by thrusting an exploring needle into the body. He will be very liable to misquote his author's meaning while he is picking off his outside sentences. He may make as great a blunder as that simple Prince, who praised the conductor of his orchestra for the piece just before the overture; the musician was too good a courtier to tell him that it was only the tuning of the instruments.

To the six propositions in the 142d paragraph, and the remarks about 'specific' diseases, the answer, if any is necessary, seems very simple. An inflammation of a serous membrane may give rise to secretions which act as a poison, whether that be a 'specific' poison or not, as Dr. Horner has told his young readers, and as dissectors know too well; and that poison may produce its symptoms in a few hours after the system has received it, as any may see in Druitt's Surgery, if they care to look. Puerperal peritonitis may produce such a poison, and puerperal women may be very sensible to its influences, conveyed by contact or exhalation. Whether this is so or not, facts alone can determine, and to facts we have had recourse to settle it.

The following statement is made by Dr. Meigs in his 142d paragraph, and developed more at length, with rhetorical amplifications, in the 134th. 'No human being, save a pregnant or parturient woman, is susceptible to the poison.' This statement is wholly incorrect, as I am sorry to have to point out to a Teacher in Dr. Meigs's position. I do not object to the erudition which quotes Willis and Fernelius, the last of whom was pleasantly said to have 'preserved the dregs of the Arabs in the honey of his Latinity.' But I could wish that more modern authorities had not been overlooked. On this point, for instance, among the numerous facts disproving the statement, the American Journal

of Medical Sciences, published not far from his lecture-room, would have presented him with a respectable catalogue of such cases. Thus he might refer to Mr. Storrs's paper 'On the Contagious Effects of Puerperal Fever on the Male Subject; or on Persons not Childbearing,' (Jan. 1846), or to Dr. Reid's case, (April, 1846,) or to Dr. Barron's statement of the children's dying of peritonitis in an epidemic of puerperal fever at the Philadelphia Hospital, (Oct. 1842), or to various instances cited in Dr. Kneeland's article, (April, 1846.) Or if he would have referred to the New York Journal, he might have seen Prof. Austin Flint's cases. Or, if he had honored my Essay so far, he might have found striking instances of the same kind in the first of the new series of cases there reported and elsewhere. I do not see the bearing of his proposition, if it were true. But it is one of those assertions that falls in a moment before a slight examination of the facts; and I confess my surprise, that a Professor who lectures on the Diseases of Women should have ventured to make it.

Nearly seven pages are devoted to shewing that I was wrong in saying I would not be 'understood to imply that there exists a doubt in the mind of any well-informed member of the medical profession, as to the fact that puerperal fever is sometimes communicated from one person to another, both directly and indirectly.' I will devote seven lines to these seven pages, which, if I may say it without offence, are, as it seems to me, six more than are strictly necessary.

The following authors are cited as sceptics by Dr. Meigs:—*Dewees*.—I cited the same passage. Did not know half the facts. *Robert Lee*.—Believes the disease is sometimes communicable by contagion. *Tonnellé* and *Baudelocque*.—Both cited by me. *Jacquemier*.—Published three years after my Essay. *Kiwisch*.—Behindhand in knowledge of Puerperal Fever.\* *Paul Dubois*.—*Scanzoni*.

Continental  
writers  
not well  
informed on  
this point.†

The story of Von Busch is of interest and value, but there is nothing in it which need perplex the student. It is not pretended that the disease is always, or even, it may be, in the majority of

\* B. & F. Med. Rev., Jan. 1842.

† See Dr. Simpson's Remarks at Meeting of Edinb. Med. Chir. Soc. (Am. Jour. Oct 1851).



cases, carried about by attendants; only that it is so carried in certain cases. That it may have local and epidemic causes, as well as that depending on personal transmission; is not disputed. Remember how small pox often disappears from a community in spite of its contagious character, and the necessary exposure of many persons to those suffering from it; in both diseases contagion is only one of the coefficients of the disease.

I have already spoken of the possibility that Dr. Meigs may have been the medium of transfer of puerperal fever in some of the cases he has briefly catalogued. Of Dr. Rutter's cases I do not know how to speak. I only ask the student to read the facts stated by Dr. Condie, as given in my Essay, and say whether or not a man should allow his wife to be attended by a practitioner, in whose hands 'scarcely a female {that has been delivered for weeks past has escaped an attack,' 'while no instance of the disease has occurred in the patients of any other accoucheur practising in the same district.' If I understand Dr. Meigs and Dr. Hodge, they would not warn the physician or spare the patient under such circumstances. They would 'go on,' if I understand them, not to seven, or seventy, only, but to seventy times seven, if they could find patients. If this is not what they mean, may we respectfully ask them to state what they do mean, to their next classes, in the name of humanity, if not of science!

I might repeat the question asked concerning Dr. Rutter's cases, with reference to those reported by Dr. Robertson. Perhaps, however, the student would like to know the opinion of a person in the habit of working at matters of this kind in a practical point of view. To satisfy him on this ground, I addressed the following question to the President of one of our principal Insurance Companies, leaving Dr. Meigs's book and my Essay in his hands at the same time.

*Question.* 'If such facts as Robertson's cases were before you, and the attendant had had ten, or even five fatal cases, or three, or *two* even, would you, or would you not, if insuring the life of the next patient to be taken care of by that attendant, expect an extra premium over that of an average case of childbirth?'

*Answer.* 'Of course I should require a very large extra premium, if I would take the risk at all.'

But I do not choose to add the expressions of indignation which the examination of the facts before him called out. I was satisfied from the effect they produced on him, that if all the hideous catalogues of cases now accumulated, were fully brought to the knowledge of the public, nothing, since the days of Burke and Hare, has raised such a cry of horror as would be shrieked in the ears of the Profession.

Dr. Meigs has elsewhere invoked 'Providence' as the alternative of accident, to account for the 'coincidences.' (Obstetrics, Phil. 1852, p. 631). If so, Providence either acts through the agency of secondary causes, as in other diseases, or not. If through such causes, let us find out what they are, as we try to do in other cases. It may be true that offences, or diseases, will come, but 'woe unto him through whom they come,' if we catch him in the voluntary or careless act of bringing them! But if Providence does not act through secondary causes in this particular sphere of ætiology, then why does Dr. Meigs take so much pains to reason so extensively about the laws of contagion, which, on that supposition, have no more to do with this case than with the plague that destroyed the people after David had numbered them? Above all, what becomes of the theological aspect of the question, when he asserts that a practitioner was 'only *unlucky* in meeting with the epidemic cases?' (Op. cit. p. 633.) We do not deny that the God of battles decides the fate of nations; but we like to have the biggest squadrons on our side, and we are particular that our soldiers should not only say their prayers, but also keep their powder dry. We do not deny the agency of Providence in the disaster at Norwalk, but we turn off the engineer, and charge the Company five thousand dollars a-piece for every life that is sacrificed. Why a grand jury should not bring in a bill against a physician who switches off a score of women one after the other along his private track, when he knows that there is a black gulf at the end of it, down which they are to plunge, while the great highway is clear, is more than I can answer. It is not by laying the open draw to Providence that he is to escape the charge of manslaughter.

To finish with all these lesser matters of question, I am unable to see why a female must necessarily be unattended in her confine-

ment, because she declines the services of a particular practitioner. In all the series of cases mentioned, the death-carrying attendant was surrounded by others not tracked by disease and its consequences. Which, I would ask, is worst,—to call in another, even a rival practitioner, or to submit an unsuspecting female to a risk which an Insurance Company would have nothing to do with?

I do not expect ever to return to this subject. There is a point of mental saturation, beyond which argument cannot be forced without breeding impatient, if not harsh feelings, towards those who refuse to be convinced. If I have so far manifested neither, it is well to stop here, and leave the rest to those younger friends who may have more stomach for the dregs of a stale argument.

The extent of my prefatory remarks may lead some to think that I attach too much importance to my own Essay. Others may wonder that I should expend so many words upon the two productions referred to, the Letter and the Lecture. I do consider my Essay of much importance so long as the doctrine it maintains is treated as a *question*, and so long as any important part of the defence of that doctrine is thought to rest on its evidence or arguments. I cannot treat as insignificant any opinions bearing on life, and interests dearer than life, proclaimed yearly to hundreds of young men, who will carry them to their legitimate results in practice.

The teachings of the two Professors in the great schools of Philadelphia are sure to be listened to, not only by their immediate pupils, but by the Profession at large. I am too much in earnest for either humility or vanity, but I do entreat those who hold the keys of life and death, to listen to me also for this once. I ask no personal favor; but I beg to be heard, in behalf of the women whose lives are at stake, until some stronger voice shall plead for them.

I trust that I have made the issue perfectly distinct and intelligible. And let it be remembered that this is no subject to be smoothed over by nicely adjusted phrases of half-assent and half-censure divided between the parties. The balance must be struck boldly and the result declared plainly. If I have been hasty,

presumptuous, ill-informed, illogical; if my array of facts means nothing; if there is no reason for any caution in the view of these facts; let me be told so, on such authority that I must believe it, and I will be silent henceforth, recognizing that my mind is in a state of disorganization. If the doctrine I have maintained is a mournful truth; if to disbelieve it, and to practise on this disbelief, and to teach others so to disbelieve and practise, is to carry desolation, and to charter others to carry it, into confiding families, let it be proclaimed as plainly what is to be thought of the teachings of those who sneer at the alleged dangers, and scout the very idea of precaution. Let it be remembered that *persons* are nothing in this matter; better that twenty pamphleteers should be silenced, or as many professors unseated, than that one mother's life should be taken. There is no quarrel here between men, but there is deadly incompatibility and exterminating warfare between doctrines. *Coincidences*, meaning nothing, though a man have a monopoly of the disease for weeks or months; or *cause and effect*, the cause being in some way connected with the person; this is the question. If I am wrong, let me be put down by such a rebuke as no rash declaimer has received since there has been a public opinion in the medical profession of America; if I am right, let doctrines which lead to professional homicide be no longer taught from the chairs of those two great Institutions. Indifference will not do here; our Journalists and Committees have no right to take up their pages with minute anatomy and tediously detailed cases, while it is a question whether or not the "black-death" of child-bed is to be scattered broadcast by the agency of the mother's friend and adviser. Let the men who mould opinions look to it; if there is any voluntary blindness, any interested oversight, any culpable negligence, even, in such a matter, and the facts shall reach the public ear; the pestilence-carrier of the lying-in-chamber must look to God for pardon, for man will never forgive him.

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Here follows, in the edition of 1855, a reprint of the paper of 1843. This is followed, in turn, by

## ADDITIONAL REFERENCES AND CASES

Fifth Annual Report of the Registrar-General of England, 1843. Appendix. Letter from William Farr, Esq.—Several new series of cases are given in the letter of Mr. Storrs, contained in the Appendix to this report. Mr. Storrs suggests precautions similar to those I have laid down, and these precautions are strongly enforced by Mr. Farr, who is, therefore, obnoxious to the same criticisms as myself.

Hall and Dexter, in *Am. Journal of Med. Sc.* for January, 1844.—Cases of puerperal fever seeming to originate in erysipelas.

Elkington, of Birmingham, in *Provincial Med. Journal*, cited in *Am. Journ. Med. Sc.* for April, 1844—Six cases in less than a fortnight, seeming to originate in a case of erysipelas.

West's Reports, in *Brit. and For. Med. Review* for October, 1845, and January, 1847.—Affection of the arm, resembling malignant pustule, after removing the placenta of a patient who died from puerperal fever. Reference to cases at Würzburg, as proving contagion, and to Keiller's cases in the *Monthly Journal* for February, 1846, as showing connection of puerperal fever and erysipelas.

Kneeland.—Contagiousness of Puerperal Fever. *Am. Jour. Med. Sc.*, January, 1846. Also, Connection between Puerperal Fever and Epidemic Erysipelas. *Ibid.*, April, 1846.

Robert Storrs.—Contagious Effects of Puerperal Fever on the Male Subject; or on Persons not Child-bearing. (From *Provincial Med. and Surg. Journal*.) *Am. Jour. Med. Sc.*, January, 1846. Numerous cases. See also Dr. Reid's case in same *Journal* for April, 1846.

Routh's paper in *Proc. of Royal Med. Chir. Soc.*, *Am. Jour. Med. Sc.*, April, 1849, also in *B. and F. Med. Chir. Review*, April, 1850.

Hill, of Leuchars.—A Series of Cases illustrating the Contagious Nature of Erysipelas and of Puerperal Fever and their Intimate Pathological Connection. (From *Monthly Journal of Med. Sc.*) *Am. Jour. Med. Sc.*, July, 1850.

Skoda on the Causes of Puerperal Fever. (Peritonitis in rab-

bits, from inoculation with different morbid secretions.) Am. Jour. Med. Sc., October, 1850.

Arneth.—Paper read before the National Academy of Medicine. *Annales d'Hygiène*, Tome LXV. 2<sup>e</sup> Partie. (Means of Disinfection proposed by M. "Semmelweis" (Semmelweiss.) Lots of chloride of lime and use of nail-brush before admission to lying-in wards. Alleged sudden and great decrease of mortality from puerperal fever. Cause of disease attributed to inoculation with cadaveric matters.) See also Routh's paper, mentioned above.

Moir.—Remarks at a meeting of the Edinburgh Medico-Chirurgical Society. Refers to cases of Dr. Kellie, of Leith. Sixteen in succession, all fatal. Also to several instances of individual pupils having had a succession of cases in various quarters of the town, while others, practising as extensively in the same localities, had none. Also to several special cases not mentioned elsewhere. Am. Jour. Med. Sc. for October, 1851. (From New Monthly Journal of Med. Science.)

Simpson.—Observations at a Meeting of the Edinburgh Obstetrical Society. (An "eminent gentleman," according to Dr. Meigs, whose "name is as well known in America as in (his) native land." *Obstetrics*. Phil. 1852, pp. 368, 375.) The student is referred to this paper for a valuable résumé of many of the facts, and the necessary inferences, relating to this subject. Also for another series of cases, Mr. Sidey's, five or six in rapid succession. Dr. Simpson attended the dissection of two of Dr. Sidey's cases, and freely handled the diseased parts. His next four child-bed patients were affected with puerperal fever, and it was the first time he had seen it in practice. As Dr. Simpson is a gentleman (Dr. Meigs, as above), and as "a gentleman's hands are clean" (Dr. Meigs' Sixth Letter), it follows that a gentleman with clean hands may carry the disease. Am. Jour. Med. Sc., October, 1851.

Peddie.—The five or six cases of Dr. Sidey, followed by the four of Dr. Simpson, did not end the series. A practitioner in Leith having examined in Dr. Simpson's house, a portion of the uterus obtained from one of the patients, had immediately afterwards

three fatal cases of puerperal fever. Dr. Peddie referred to two distinct series of consecutive cases in his own practice. He had since taken precautions, and not met with any such cases. *Am. Jour. Med. Sc.*, October, 1851.

Copland.—Considers it proved that puerperal fever may be propagated by the hands and the clothes, or either, of a third person, the bed-clothes or body-clothes of a patient. Mentions a new series of cases, one of which he saw, with the practitioner who had attended them. She was the sixth he had had within a few days. All died. Dr. Copland insisted that contagion had caused these cases; advised precautionary measures, and the practitioner had no other cases for a considerable time. Considers it criminal, after the evidence adduced,—which he could have quadrupled,—and the weight of authority brought forward, for a practitioner to be the medium of transmitting contagion and death to his patients. Dr. Copland lays down rules similar to those suggested by myself, and is therefore entitled to the same epithet for so doing. *Medical Dictionary*, New York, 1852. Article, Puerperal States and Diseases.

If there is any appetite for facts so craving as to be yet unappeased,—*lassata, necdum satiata*,—more can be obtained. Dr. Hodge remarks that “the frequency and importance of this singular circumstance (that the disease is occasionally more prevalent with one practitioner than another) has been exceedingly over-rated.” More than thirty strings of cases, more than two hundred and fifty sufferers from puerperal fever, more than one hundred and thirty deaths appear as the results of a sparing estimate of such among the facts I have gleaned as could be numerically valued. These facts constiute, we may take it for granted, but a small fraction of those that have actually occurred. The number of them might be greater, but “ ‘t is enough, ‘t will serve,” in Mercutio’s modest phrase, so far as frequency is concerned. For a just estimate of the importance of the singular circumstance, it might be proper to consult the languid survivors, the widowed husbands, and the motherless children, as well as “the unfortunate accoucheur.”

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PERCIVALL POTT, 1714-1788

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## Percivall Pott

English Physician, 1714-1788

### BIOGRAPHY

- 1714 Born January 6, in Threadneedle St., London. Son of a London scrivener. Father died when Percivall was 3 years old, leaving family in straitened circumstances.
- 1729 Age 15. Apprenticed to Edward Nourse, assistant surgeon to St. Bartholomew's Hospital.
- 1736 Age 22. Admitted into Freedom of Barber's Company by service as apprentice in preparing anatomical specimens for demonstration by Dr. Edward Nourse.
- 1739 Age 25. Took livery of Barber Surgeon's Company.
- 1744 Age 30. Appointed assistant surgeon to St. Bartholomew's Hospital, London.
- 1745 Age 31. Became active member of Corporation of Surgeons.
- 1749 Age 35. Became Full Surgeon to St. Bartholomew's.
- 1753 Age 39. Appointed, with John Hunter, lecturer on Anatomy at St. Bartholomew's.
- 1756 Age 42. Suffered fracture of leg. (There is a controversy as to whether it was actually a so-called Pott's Fracture.) Enforced leisure turned his energies to writing of books; he published many volumes and had several of his works translated into French, Italian, German and Dutch.
- 1760 Age 46. Described Puffy Tumor (Pott's).
- 1764 Age 50. Elected Fellow of the Royal Society.
- 1765 Age 51. Became Master, or Governor, of Corporation of Surgeons.

- 1768 Age 54. Described fracture of leg (Pott's fracture).  
 1779 Age 65. Described caries of spine (Pott's disease). Had largest surgical practice in London. His lectures drew many foreign pupils to St. Bartholomew's.  
 1786 Age 72. Given Honorary Fellowship by Royal College of Surgeons in Edinburgh. Elected Honorary Member by the Royal College of Surgeons of Ireland.  
 1787 Age 73. Resigned as surgeon to St. Bartholomew's Hospital which he had served, according to his own words, "as man and boy, for half a century."  
 1788 Age 74. Died of pneumonia, December 22, and was buried in the chancel of St. Mary's, Aldermary, in Queen Victoria Street.

## EPONYMS

1. DISEASE: Osteitis or caries of the vertebrae, usually of tuberculous origin. (1st paper) *Remarks on That Kind of Palsy of the Lower Limbs Which is Frequently Found to Accompany a Curvature of the Spine and is Supposed to be Caused by it, Together with its Method of Cure.* 84 pp., 8°, London, J. Johnson, 1779. Also: *Surgical Works*, London, Wood & Innes, 3: 229-258, 1808. (2nd paper) *Further Remarks on the Useless State of the Lower Limbs, in Consequence of a Curvature of the Spine; Being a Supplement to a Former Treatise on That Subject.* 64 pp., 6 pl., 8°, London, J. Johnson, 1782. Also: *Surgical Works*, London, Wood & Innes, 3: 259-296, 1808.
2. FRACTURE: Of the lower part of the fibula, with serious injury of the lower tibial articulation, usually a chipping off of a portion of the inner malleolus, or rupture of the internal lateral ligament. *Some Few General Remarks on Fractures and Dislocations.* London, Hawes, pp. 57-64, 1769. Also: *Surgical Works*, London, Wood & Innes, 1: 325-331, 1808.
3. PUFFY TUMOR: A circumscribed edema of the scalp associated with osteomyelitis of the skull bones. *Observations on the Nature and Consequences of Wounds and Contusions of the*

*Head, Fractures of the Skull, Concussions of the Brain, etc.*  
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B—New York State Library.

C—New York Academy of Medicine Library.

D—Brooklyn Academy of Medicine Library.

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4. Observations on the Nature and Consequences of Wounds and Contusions of the Head, Fractures of the Skull, Concussions of the Brain, etc. xxxii, 182 pp., 8°, London, Hitch and Hawes, 1760, in A.
5. Practical Remarks on the Hydrocele, or Watery Rupture, and Some Other Diseases of the Testicle, its Coats, and Vessels (Illustrated with Cases); Being a Supplement to a General Treatise on Ruptures, Published in the Year

- MDCCLVI. vii, 223 pp., 8°, London, Hitch and Hawes, 1762, in A. Same, 2nd ed., vii, 2 pl., 327 pp., London, Hawes, 1767, in A, B, C & E. Same, *Abhandlung von dem Wasserbruch und andern Krankheiten des Hoden, seiner Häute und seiner Gefässe. Mit vielen Fällen erläutert. Nach der 2. verbesserten und vielvermehrten Ausg. übersetzt, von Johann Clemens Tode.* 5 p. l., 324 pp., 8°, Kopenhagen, Rothe, 1770, in A. Same, 3rd ed., London, Hawes, 1773, in D & E.
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## POTT'S DISEASE

Tuberculosis of the spine is one of the oldest diseases known to medicine because it produces changes in the skeleton which lead to a correct diagnosis centuries after the patient has died. Eliot Smith has found many examples in Egyptian mummies and Sudhoff and Sticker describe a case in a mummy of the 21st Dynasty in *Zur historischen Biologie der Krankheitserreger*, Giessen, 1910. See also Ruffer, *Palaeopathology of Egypt*, Chicago University Press, 1921, p. 3.

Hippocrates guessed the tuberculous nature of gibbous spine (*On the Articulations*, Par. 41). Galen confirmed Hippocrates. A study of the condition was revived by J. Z. Platner in 1774, and advanced by Delpech in 1816. (Garrison, *History of Medicine*, 4 ed., Phila., Saunders, 1929, p. 344.)

In the meantime, in 1779, Percival Pott published his first *Remarks on that Kind of Palsy of the Lower Limbs which is Frequently Found to Accompany a Curvature of the Spine and is Supposed to be Caused by it* (see following pages). The essay does not attempt to describe the disease completely nor did Pott recognize its tuberculous nature but he did describe the deformity and its sequelae. He recalls a conversation with a Dr. Cameron who told him of similar cases mentioned by Hippocrates where a cure was obtained by an abscess draining in the back or loins. Therefore Potts recommended treatment of the leg palsy and spinal curvature by "merely procuring a large discharge of matter, by supuration, from underneath the membrana adiposa on each side of the curvature." He reported several successful outcomes with this treatment.

A more complete account of tuberculosis of the spine was published in the same year, 1779, by Jean-Pierre David, for whom the condition should properly be named, David's disease of the spine. This is simply one example of the well-known fact that a disease is not always named after its discoverer or the most deserving man. Advertising, preferably by one's friends, also pays in medical history.

In 1882 Pott published *Further Remarks on Palsy of the Lower Limbs*, etc. (see following pages), including six plates illustrating the pathology of the condition. He acknowledged confirmation of his successful treatment by other practitioners. In this essay he recognized a relationship between the disease of the spine he was describing and scrofula in other parts of the body and described in detail most of the clinical and pathological findings as we now know them.

Not until 1882 when Robert Koch discovered the tubercle bacillus was the true etiology of Pott's disease of the spine established.

Modern interest in Pott's disease has centered largely in surgical intervention to stabilize the spine. In 1911 F. H. Albee suggested transplantation of a portion of the tibia into the split spinous processes (*Jour. Amer. Med. Assn.*, 57: 885-6) and in the same year R. A. Hibbs recommended overlapping fractures of the spinous processes at their bases (*N. Y. Med. Jour.*, 93: 1013-6).



REMARKS

ON THAT KIND OF

PARALYSIS

OF THE

LOWER LIMBS,

WHICH IS FREQUENTLY FOUND TO ACCOMPANY  
A CURVATURE OF THE SPINE,  
AND IS SUPPOSED TO BE CAUSED BY IT.

TOGETHER WITH

ITS METHOD OF CURE.

TO WHICH ARE ADDED,

OBSERVATIONS on the NECESSITY and  
PROPRIETY of AMPUTATION,  
IN CERTAIN CASES,  
AND UNDER CERTAIN CIRCUMSTANCES.

By PERCIVALL POTT, F. R. S.

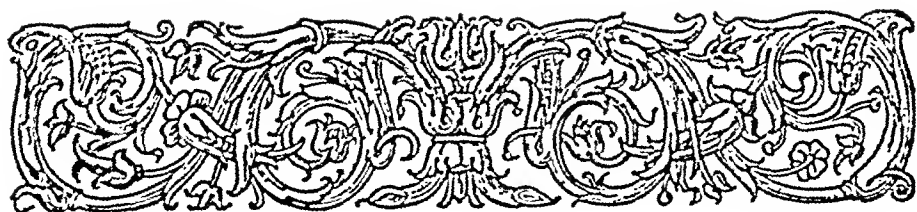
And SURGEON to ST. BARTHOLOMEW'S HOSPITAL,

*Verumque est ad ipsam curandi rationem nihil plus conferre  
quam experientiam.*

CELSUS.

L O N D O N :

Printed for J. JOHNSON, No. 72, St. Paul's Church-Yard,  
M,DCC,LXXIX.



# Remarks on That Kind of Palsy of the Lower Limbs Which Is Frequently Found to Accom- pany a Curvature of the Spine, and Is Supposed to Be Caused by It, Together with Its Method of Cure

BY

PERCIVALL POTT, F.R.S.

*Surgeon to St. Bartholomew's Hospital*

**A**MONG the various objects of Physick and Surgery, there are unfortunately some in which all the efforts of both, have hitherto been found absolutely ineffectual, and which therefore have always made a very disagreeable, and melancholy part of practice.

To be able to remove, or even to relieve any of the various miseries, to which mankind are liable, is a very satisfactory employment; but to attend on a distemper from its beginning, through a long and painful course, to its last, fatal period, without even the hope of being able to do any thing which shall be really serviceable, is, of all tasks the most unpleasant.

In such cases, any attempts, however hazardous, provided they were in any degree rational, would be justifiable; certainly then,

whatever is not in itself dangerous, and affords the smallest ray of hope, ought to be embraced.

Some little time ago I gave to the public an account of the success which I had seen attend the free use of opium in mortifications of the toes and feet; particularly in those which began, or were attended with great pain.

In that publication I merely related the fact, as it had happened under my own eye; I entered into no reasoning about it; not did I give to the medicine any greater degree of credit than it appeared to me to deserve; I did not propose it as a certain specific, or as a remedy whose success was always and infallibly, or indeed even generally to be depended upon; I acknowledged, that I had several times seen it fail; but as I had also several times seen it succeed, as I was very sure that no hazard could possibly attend the experiment, and, as the best and most experienced practitioners were obliged to allow, that they were not yet acquainted with any means whereby they were enabled to prevent the fatal effects of this most horrid distemper, or even to retard its daily and painful ravages, I thought it my duty to make known as early as I could, what I had seen, that others might make the same trial, and thereby propagate the benefit. Had any other means of relief been known to the faculty, and this had therefore appeared to me only in the light of another, or a preferable one, I should certainly have withheld my observations, until more time had verified and confirmed them, and thereby have proved the superior utility of what I had to propose: but as the fact was directly the contrary, as opium was the only medicine which I had ever seen prove really, and essentially serviceable; as it had succeeded so often, and to such a degree, as to satisfy me that much good might be expected from it; and as I was perfectly sure that not the least degree of hazard could attend the trial, I thought that such publication, though early, could not be regarded in any other light than its true one; I mean that of a request to the profession in general to repeat the experiment; and that therefore it could not be justly deemed premature. If upon repeated trial the success should not be

found equal to what I thought I had good reason to expect, no harm could accrue to the patient; if it should answer my expectation, it would serve the most valuable of all purposes.

Since that time I have had the satisfaction of having my opinion confirmed, not only by my own experience, but by the concurrent testimony of several practitioners of eminence in different parts of the kingdom, who have done me the favor to communicate to me the result of their experiments; the success of these, as I expected, from what I had seen, have not been constant, but it has been so frequent, as to make me very well pleased at having furnished the hint. I sincerely wish that the good effect was more general and more certain, but the preservation of even a few, from a malady, found hitherto to have been inevitably destructive to all, is a matter of some importance, and furnishes no unpleasing reflection.

I now do the same thing, relative to another disorder, which I then did with regard to the mortification. I publish an account of the good success which has attended a particular method of treating a disease, which has hitherto foiled all the efforts of art; and as I do it now from the same principle which I did then, *viz.* that of inducing others, by making the same experiment, to propagate the benefit, I make no apology for another early publication.

The disease of which I mean to speak, is generally called a palsy, as it consists in a total or partial abolition of the power of using, and sometimes of even moving the lower limbs, in consequence, as is generally supposed, of a curvature of some part of the spine.

To this distemper both sexes, and all ages, are equally liable. If the patient be an infant, it becomes an object of constant, though unavailing distress to its parents; if an adult, he is rendered perfectly helpless to himself, and useless to all others, which, of all possible states, is surely the very worst.

When this disease attacks an infant of only a year or two old, or under, the true cause of it is seldom discovered until some time after the effect has taken place, at least not by parents and nurses,



who know not where to look for it. The child is said to be uncommonly backward in the use of his legs, or it is thought to have received some hurt in its birth.

When it affects a child who is old enough to have already walked, and who has been able to walk, the loss of the use of his legs is gradual, though in general not very slow. He at first complains of being very soon tired, is languid, listless, and unwilling to move much, or at all briskly; in no great length of time after this he may be observed frequently to trip, and stumble, although there be no impediment in his way; and whenever he attempts to move briskly, he finds that his legs involuntarily cross each other, by which he is frequently thrown down, and that without stumbling; upon endeavoring to stand still and erect, without support, even for a few minutes, his knees give way and bend forward. When the distemper is a little farther advanced, it will be found that he cannot, without much difficulty and deliberation, direct either of his feet precisely to any exact point; and very soon after this, both thighs and legs lose a good deal of their natural sensibility, and become perfectly useless for all the purposes of locomotion. When an adult is the patient, the progress of the distemper is much the same, but rather quicker.

Until the curvature of the spine has been discovered, it generally passes for a nervous complaint; but when the state of the back bone has been adverted to, recourse is almost always had to some previous violence to account for it; some pulling, lifting, carrying, or drawing a heavy body, which is supposed to have hurt the back. In some few instances, this exertion may have been such, as might be allowed to have been equal to the effect, but, in by much the majority, this is so far from being the case, that if it be admitted to have had any share at all in it, some predisposing cause, at least, must be looked for, in which, (in my opinion) consists the very essence of the disease.

I have, in compliance with custom, called the disease a palsy; but it should be observed, that notwithstanding the lower limbs be rendered almost, or totally useless, yet there are some essential circumstances in which this affection differs from a common nervous palsy: the legs and thighs are, I have just said, rendered

unfit for all the purposes of locomotion, and do also lose much of their natural sensibility, but notwithstanding this, they have neither the flabby feel, which a truly paralytic limb has, nor have they that seeming looseness at the joints, nor that total incapacity of resistance, which allows the latter to be twisted in almost all directions; on the contrary the joints have frequently a considerable degree of stiffness, particularly the ankles, by which stiffness the feet of children are generally pointed downward, and they are prevented from setting them flat upon the ground.

The curvature of the spine, which is supposed to be the cause of this complaint, varies in situation, extent and degree, being either in the neck or back, and sometimes (though very seldom) in the upper part of the loins; sometimes comprehending two vertebrae only, sometimes three, or more, by which the extent of the curve becomes necessarily more or less; but whatever may be the number of vertebrae concerned, or whatever may be the degree or extent of the curvature, the lower limbs only feel the effect—at least I have never once seen the arms affected by it.

This effect is also different in different subjects: some are rendered totally and absolutely incapable of walking in any manner, or with any help, and that very early in the course of the distemper; others can make a shift to move about with the help of crutches, or by grasping their own thighs with their hands; some can sit in an erect posture, or in a chair, without much trouble or fatigue, which others are incapable of, at least for any length of time; some have such a degree of motion in their legs and thighs, as to enable them to turn and move for their own convenience in bed, others have not that benefit, and are obliged to lie till moved by another.

When a naturally weak infant is the subject, and the curvature is in the vertebrae of the back, it is not infrequently productive of additional deformity, by gradually rendering the whole back what is commonly called humped; and by alterations which all the bones of the thorax sometimes undergo, in consequence of the flexure and weakness of the spine, by which such persons are justly said to be shortened in their stature; but in all cases where

this effect has been gradually produced, to whatever degree the deformity may extend, or however the alteration made in the disposition of the ribs and sternum may contribute to such deformity, yet I think that it will always be found, that the curvature of the spine appeared first, and, if I may so say, singly, and that all the rest was consequential.

While the curvature of the spine remains undiscovered or unattended to, the case is generally supposed to be nervous, and medicines so called are most frequently prescribed, together with warm liniments, embrocations, and blisters, to the parts affected; and when the true cause is known, recourse is always had to steel stays, the swing, the screw chair, and other pieces of machinery, in order to restore the spine to its true and natural figure; but all, as far as I have observed, to no real or permanent good purpose; the patient becomes unhealthy, and languishing for some time under a variety of complaints, dies in an exhausted, emaciated state; or, which is still worse, drags on a miserable existence, confined to a great chair, or bed, totally deprived of the power of locomotion, and useless both to himself and others.

This in an infant is most melancholy to see, in an adult most miserable to endure.

The general health of the patient does not seem at first, to be materially, if at all, affected, but when the disease has been some time, and the curvature thereby increased, many inconveniences and complaints come on, such as difficulty in respiration, indigestion, pain, and what they all call tightness at the stomach, obstinate constipations, purgings, involuntary flux of urine and faeces, &c. with the addition of what are called nervous complaints; some of which are caused by the alterations made in the form of the cavity of the thorax, others seem to arise from impressions made on the abdominal viscera. These are different both in kind, and in degree, in different subjects, but seem to depend very much on the consequences of the curvature—that is, in naturally infirm children, although the curvature of the dorsal vertebrae is always the first mark of the distemper, by preceding every other, yet it is frequently soon followed by such a degree of deformity of the bones of the trunk, as to be, in conjunction with

the necessary inactivity and confinement of the patient, productive of all the ills above-mentioned.

An affecting instance of this distemper in the person of a very promising youth of fourteen years old, with whose family I was nearly connected, induced me to think more of it than perhaps I otherwise should have done; and the restoration of the use of his limbs, immediately after a seemingly accidental abscess near the part, engaged my attention still more, and became a matter of frequent, though not very satisfactory contemplation; I say unsatisfactory, because it served only to increase my doubts, without leading me toward a solution of them. The more I thought upon the subject, the more I was inclined to suspect that we had been misled by appearances, and that a distempered state of the parts forming, or in the neighbourhood of curvature, preceded, or accompanied it: in short, that there was something predisposing, and that we had most probably mistaken an effect for a cause.

For these suspicions, I had the following reasons, which appeared to me to have some weight:

1. That I had never seen this paralytic effect on the legs from a malformation of the spine, however crooked such malformation might have rendered it, or whether such crookedness had been from time of birth, or had come on at any time afterwards during infancy.

2. That none of those strange twists and deviations, which the majority of European women get in their shapes, from the very absurd custom of dressing them in stays during their infancy, and which put them into all directions but the right, ever caused any thing of this kind, however great the deformity might be.

3. That the curvature of the spine, which is accompanied by this affection of the limbs, whatever may be its degree, or extent, is at first almost always the same, that is, it is always from within, outward, and seldom or never to either side.

4. That since I had been particularly attentive to the disorder, I had remarked, that neither the degree nor the extent of the curve, made any alteration in the nature or degree of the symptoms at first, nor for some time after the appearance; or, in

other words, that the smallest curvature, in which only two or three of the vertebrae were concerned, was always, at first, attended by the same symptoms as the largest.

5. That although it sometimes happened that a smart blow, or a violet strain had immediately preceded the appearance of the curve, and might be supposed to have given rise to it, yet in many more adults it happened that no such cause was fairly assignable, and that they began to stoop, and to falter in their walking, before they thought at all of their back, or of any violence offered to it.

6. That exactly the same symptoms are found in infants, and in young children, who have not exerted themselves, nor have been injured by others, as in the adult, who has strained himself, or received a blow; and that the case was still the same in those grown people, who have neither done, nor suffered any act of violence.

7. That although it must be allowed, that a dislocation of any of the vertebrae, would most probably be attended with the same kind of symptoms from the pressure it must make on the spinal marrow, yet it is also most probable that such symptoms would be immediate, and attended with great pain in the part; neither of which is in general the case here.

These considerations appeared to me to have much force; but what confirmed me in my opinion was the state of the parts forming the curvature, and which I had several fair opportunities of examining after death. By these examinations I found in infants, in young children, and in those who had been afflicted with the disorder but a small space of time, that the ligaments connecting the vertebrae, which formed the curve, were in some degree altered from a natural state, by being somewhat thickened and relaxed, and that what are called the bodies of those bones, were palpably spread and enlarged in their texture, just as the bones forming the articulations are in children who are called rickety. That in those who had long labored under the distemper, and in whom the symptoms were aggravated, whatever might be their age, the ligaments were still more thickened, relaxed, and altered, the bodies of the bones more spread, more

enlarged, and more inclining to become carious, and the cartilages between the bodies of the vertebrae much compressed and lessened in size; and that in all those who had so long labored under the disease, as to have been destroyed by it, or by its consequences, the corpora vertebrarum were completely carious, the intervening cartilages totally destroyed, and a quantity of sanies lodged between the rotten bones, and the membrane investing the spinal marrow.\*

All these circumstances put together, induced me, as I have already said, to suspect, that when we attribute the whole of this mischief to the mere accidental curvature of the spine, in consequence of violence, we mistake an effect for a cause, and that previous both to the paralytic state of the legs, and to the alteration of the figure of the back bone, there is a pre-disposing cause of both, consisting in a distempered state of the ligaments and bones, where the curve soon after makes its appearance.

While the subject was fresh in my mind, I happened to be at Worcester, and in a conversation on it with the late Doctor Cameron of that place, I mentioned to him my opinion, and my doubts; the Doctor concurred with me, and at the same time mentioned a circumstance, which made a strong impression on me. He said, that he remembered some years ago, to have noted a passage in Hippocrates, in which he speaks of a paralysis of the lower limbs being cured by an abscess in the back or loins, and that taking the hint from this, he, Dr. Cameron, had, in a case of a palsy of the legs and thighs, attended by a curvature of the back bone, endeavored to imitate this act of nature, by exciting a discharge near the part, and that it had proved very advantageous. He also referred me to Mr. Jeffrys, a surgeon of eminence at Worcester, for a farther account of the same kind of attempt; this gentleman confirmed what Dr. Cameron had told me, and assured me that he had found the method equally successful.

It may easily be supposed, that these accounts from gentlemen

\* In the body of a man who died not long since, of this disorder, in its last and worst state, the bodies of three of the vertebrae were not only quite carious, but completely separated from all connections with the other parts of the same vertebrae.

of veracity, and of reputation in their profession, still added to my desire of knowing more on this subject, and determined me to lose no opportunity of getting information.

The first that offered was in an infant, whose curvature was in the middle of the neck, and who had lost the use of its legs for about two or three months. I made an issue by incision on one side of the projection, and gave strict charge to the mother to take care that the pea was kept in; the woman, who had no faith in the remedy, did not take the proper care, and consequently the discharge was not equal to what it should, and might have been; but notwithstanding this neglect, at the end of about three weeks or a month the child was manifestly better, and began to make use of its legs; it was then seized with the small-pox and died. The bodies of the vertebrae concerned in the curve, were larger than they should be, and than those above and below were, and their texture much more open and spongy, which difference appeared immediately, before the parts covering them were dissected off.

Some time passed before I had another opportunity. My next patient was a tall thin man, about thirty-five years old, who thought that he had hurt himself by lifting a heavy weight: his legs and thighs were cold, and what he called nummy, but not absolutely useless: he could with difficulty go about the room with the help of a pair of crutches, but he could neither rise from his chair, nor get on his crutches without the assistance of another person, nor could he without them walk at all.

I made a seton on each side of the curve, which was in his back, about the middle, and having given his wife directions how to dress them, I called on him once in three or four days. At the end of six weeks he had recovered the due degree of sensation in his limbs, and found much less necessity for the use of his crutches; he could rise from his bed, and from his chair without assistance, and by means of one crutch, and an underhand stick, could walk for an hour, or more, without resting, and without fatigue. The setons had now, from not having been properly managed, worn their way out, and I would have converted each of them into an issue, but as neither the patient nor his wife had ever believed

that the discharge had had any share in his amendment, but on the contrary that he would have been better without it, he would not submit to what I proposed, and I left him. At the distance of about three weeks from the time of my leaving him, I met him in the street walking very stoutly, with a common cane, of which he made little or no use. I asked him what he had done: he told me that the sores had continued to discharge till within a few days, but that he had drank a great deal of comfrey-root tea, with isinglass, and he supposed that had cured him.

I believe that the cure of this man will, by all who know any thing of medicine, be thought to be so unlikely to have been affected by the comfrey and isinglass, that my inference in favour of the seton will not be thought unreasonable, and that my determination to prosecute the method, from what I had heard and seen, was well founded.

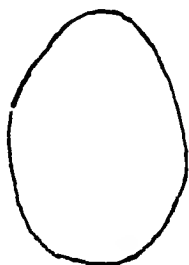
Within the course of the last ten or twelve months, I have had several fair opportunities of doing this, both in St. Bartholomew's hospital, and out of it, and am very happy to be able to say, that it has not only always answered, but in some instances greatly exceeded my most sanguine expectations, by restoring several most miserable and totally helpless people to the use of their limbs, and to a capacity of enjoying life themselves, as well as of being useful to others.

I have now in the hospital a boy about twelve years old, whose case was so truly deplorable, that I made the experiment merely to avoid the appearance of inhumanity, by discharging him as incurable, without trying something. The curvature was in his back, and consisted of three or four vertebrae, but by means of the weakness thereby induced, the whole set of dorsal ones had so universally and gradually given way, that he was exceedingly deformed both behind and before: he was so absolutely incapable of motion, that he could neither turn himself, nor sit up in his bed: his feet were pointed downwards, and his ankles so stiff, that when he was held up under the arms, the extremities of his great toes touched the floor, nor could his feet be brought flat to the ground by any means, or force whatever. In short, he was as perfectly and as totally helpless as can be supposed, and at the



same time in an exceeding general bad state of health, from disorders of the thoracic and abdominal viscera. In this state he had been more than a year: it is now about three months since the caustics were applied; he is become healthy, and free from most of his general complaints, has the most perfect use of his legs while he is in bed, can walk without the assistance of any body, or any thing to hold by; and from his manner of executing this, will, I make no doubt, in a very short space, recover perfectly the use of his legs—To this I ought to add, that notwithstanding a considerable degree of deformity does, and I suppose will, remain, yet the spine in general is so much strengthened, that he is some inches taller than he was four months ago.

The remedy for this most dreadful disease consists merely in procuring a large discharge of matter, by suppuration from underneath the membrana adiposa on each side of the curvature, and in maintaining such discharge until the patient shall have perfectly recovered the use of his legs. To accomplish this purpose, I have made use of different means, such as setons, issues made by incision, and issues made by caustic; and although there be no very material difference, I do upon the whole prefer the last. A seton is a painful and a nasty thing, beside which it frequently wears through the skin before the end for which it was made can be accomplished: issues made by incision, if they be large enough for the intended purpose, are apt to become inflamed, and to be very troublesome before they come to suppuration; but openings made by caustic are not in general liable to any of these inconveniences, at least, not so frequently, nor in the same degree: they are neither so troublesome to make or to maintain. I make the eschars about this size and shape on each side the curve,



taking care to leave a sufficient portion of skin between them; in a few days, when the eschar begins to loosen and separate, I cut out all the middle, and put into each a large kidney-bean: when the bottoms of the sores are become clean by suppuration, I sprinkle every third or fourth day, a small quantity of finely powdered cantharides on them, by which the sores are prevented from contracting, the discharge increased, and possibly other benefit obtained. The issues I keep open until the cure is complete, that is, until the patient recovers perfectly the use of his legs, or even for some time longer, and I should think that it would be more prudent to heal only one of them first, keeping the other open for some time, that is, not only until the patient can walk, but until he can walk firmly, briskly, and without the assistance of a stick; until he can stand quite upright, and has recovered all the height, which the habit, or rather the necessity of stooping occasioned by the distemper, had made him lose.

I have said that the discharge by means of the issue, is all that is requisite for a cure, which is true, as I have experimentally proved by not using any other, in cases which have succeeded perfectly; but this fact being established, there is no reason why every assistant means should not be applied at the same time, in order to expedite: such as bark, cold-bathing, frictions, &c.

That the patient becomes more upright as his legs become stronger, is certain, and therefore appears taller, as well as straighter in proportion, as the whole spine strengthens; but whether the curvature will always and totally disappear, I am not yet able to say with certainty. In two late instances, both adults, it has, but the deformity, which in weak infants and children, is often the consequence of the curvature, and of the state of the spine at that place, must in some degree, I fear, be expected to remain; but of this I am not yet able to speak with absolute certainty. There are a few other circumstances, of no great moment perhaps, but which will require more time to ascertain than I thought should be suffered to pass, before mankind were made acquainted with the great means of relief, in so distressing, so melancholy, and so dreadful a malady: for the

reader will be pleased to remember what I told him at the beginning of this tract, which was, that my motive for publishing this account sooner than might appear in general to be right, or indeed than I otherwise should have done, was a desire that as little time as possible might be lost, in conveying to the profession in particular, and to mankind in general, the means of relief under an affliction, which, till these were known, has not admitted of any: and this I was still more incited to do, because the remedy is as harmless, and as void of hazard, as it is efficacious.

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In the preceding tract I have related the appearances which the parts constituting the seat of the distemper make upon examination after death; or to speak more properly, the different states of these parts in different persons, and at different periods of this disease. These, though necessarily subject to considerable variety, may, I think, be reduced to three general ones.

1. A small degree of an increase of size in the bodies of the vertebrae, forming the curve, with an apparent laxity in their texture, and a relaxed state of the connecting ligaments, by which they seem to have lost part of their power of holding the bones together.

2. A more considerable, and more apparent enlargement of the same parts of the vertebrae, whose spongy texture becomes more visibly spread through their whole substance, and tending towards a caries, with an apparently distempered state, both of the ligaments, and of the intervening cartilages.

3. A truly carious state of the bodies of the bones, a dissolution, or destruction of the cartilaginous substance between them, and a lodgement of sanies on the surface of the membrane enveloping the spinal marrow.

These are I think the most particularly different states or stages of the disorder, and are such as, in my opinion, decisively mark the true nature of it.

Between these in different persons, and under different circumstances, there must be a considerable variety, but the material difference will be only in degree.

From the whole, the few following practical inferences seem fairly deducible.

1. That the disease does not originally consist in a displacement of the vertebrae, made by violence, the bones and ligaments being previously in a sound and uninjured state; but in such a morbid alteration of the texture of both, as will, if not timely prevented, produce curvature and caries, with all their consequences.

2. That the proper remedies for this disease cannot be applied too soon.

3. That the restoration of the spine to its natural figure, depends much on the early administration of the help proposed.

4. That although the distemper may be so far cured, that the patient may perfectly recover the use of his legs, yet such an alteration may have taken place in the bodies of the vertebrae, as to render it impossible for the spine to become straight again.

5. That when three or four, or more vertebrae, are concerned in the curve, the trunk of the body will have so little support from that part of the spine which is not distempered, that no degree of deformity can be wondered at; nor can it be expected that such deformity should be removed, whatever other benefit such patient may receive.

6. That if from inattention, from length of time, or from any other circumstances, it happens that the bodies of the vertebrae become completely carious, and the intervening cartilages are destroyed, no assistance is to be expected from the proposed remedy.

To these I will take the liberty of adding, that it appears to me well worth while, to try what a large and free discharge, made for a length of time from the vicinity of the distempered part, might be capable of doing in the very beginning of what are commonly called scrophulous joints; which when arrived to a certain point, baffle all our art, and render a painful and hazardous operation, absolutely necessary.

Within these last six or eight months, several cases of curved spine have been received into St. Bartholomew's hospital, where they have been seen by great numbers of the profession. The novelty of the treatment, and the success which has hitherto

constantly attended it, has necessarily engaged the attention of many, and occasioned some conversations on the subject. In some of these it has been said, that as it appears to be undeniably a disease of the bony texture of the bodies of the vertebrae, it may be apprehended, that the relief expected from the caustics, may, in some cases, fail, and in others may not prove permanent; and, that the same kind of constitution remaining, a return of the malady may not unreasonably be feared.

To this I can only answer, that although I have called this an early publication, yet I have waited a sufficient length of time, and have treated a sufficient number of subjects, to be clear in the truth of what I have asserted as far as such time, and such individuals go. That the patients whom I have attended in the early part of the distemper of whatever age, have all got well: that is have all not only regained the use of their legs, but have become healthy, and fit for any exercise or labour, as numbers can testify, who have seen them daily. Most of them have become much straiter, some quite strait, and all of them perfectly free from all kind of inconvenience arising from the Curve.

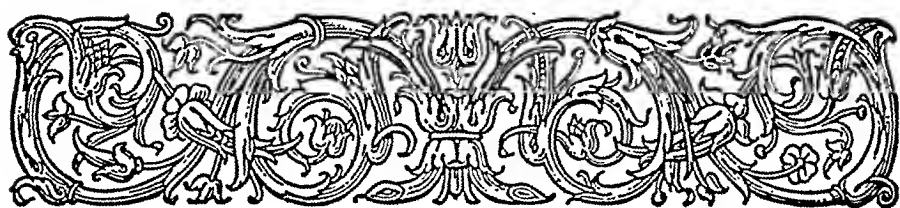
That in all the infants whom I have seen, the general health of the patient has always been restored in proportion to the restoration of the use of the limbs.

That I must suppose all this to have been done by the discharge from the caustics, because in many of them no other means of any kind have been made use of.

That as far as my experience goes I have not the least doubt, that if the means proposed, be made use of before the bones are become really carious and rotten, that they will always be successful. When indeed a truly rotten state of the bones takes place no good is to be expected from this or from any thing else: but it should be observed at the same time, that this never happens but when the distemper is of very old date, and that when this is the case, the whole machine is so disordered, and the patient so truly and so generally distempered, that there can be no reasonable expectation of success from any thing.

To this I must take the liberty of adding, that what I have affirmed, is what I have seen and proved, and that the objections

are merely speculative and theoretical. However, supposing them to be not quite unreasonable, the most useful inference to be drawn from them is, that the same remedy by which so great and so evident relief is obtained ought to be continued, while there may be any fear of return of the mischief, and that every other means for the restoration of health and strength should at the same time be made use of; both which coincide absolutely with my own opinion and advice.



# Further Remarks on the Useless State of the Lower Limbs in Consequence of a Curvature of the Spine

BY

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**I**T IS now near three years since I first troubled the public with my observations on the disease which makes the subject of the following tract. The apology which I then made, for what I was perfectly aware might be thought a premature publication, was, that the distemper to which it related was supposed to be incapable of receiving any relief from art; and that they who were afflicted with it were therefore deserted, and left to linger out a most miserable existence; but, that from the benefit which I had seen to be derived from a particular, and at the same time a perfectly safe method of treating it, I thought that it demanded the immediate and serious regard of the profession.

Previous to the publication, I had considered the disease with some attention, and had made some experiments on it, which, although not many, were sufficient in number, and had been attended with such a degree of success as to satisfy me, that it was a subject in which mankind was much interested; but as I did not think that any one man's experience, be it what it might, was sufficient to determine a matter of so much importance, I

wished that the faculty at large might be made acquainted with what I had seen and done, that they might be induced to make the same experiment, and thereby either contradict or confirm what I had said; if the former should be the result, my proposition would soon meet with the neglect which it would deserve; I could only console myself with the rectitude of my intention, and be sorry for my mistake: but if, on the contrary, the attempts of others should prove as successful as mine, it appeared to me, that the chirurgic art would make a great acquisition, as it would be thereby furnished with the means of relieving one of the most distressing maladies to which human nature is liable; a malady which, when it befalls an adult, makes him compleatly miserable, by depriving him of all power of being useful to himself or others; a malady which, when an infant becomes its victim, renders all the care and tears, all the tenderness and anxiety of the fondest parent absolutely unavailing, and a malady for which it was supposed, there was no remedy.

These were my reasons for hazarding my opinion so hastily: the importance of the subject, and the perfect safety of the experiment, were, as I thought, a sufficient excuse for so doing.

My wishes, and my expectations, have been most pleasingly fulfilled. I have received such manifold and repeated testimony of the success of the proposed method, from so large a number of the most eminent practitioners, not only in this town and kingdom, but in many other parts of Europe; that these, added to my own experience, have completely satisfied me, and enabled me to say, that in proper cases, and under proper treatment, I have no doubt of its being universal.

In all the time which has passed since the first publication, I have sought and embraced every opportunity of obtaining information, both from the living and from the dead; and I have requested and received the assistance of many friends, whose civilities, and whose information, I take this opportunity of acknowledging.

By these means I have been enabled to correct several errors, and to make some additional observations, which I hope may not only elucidate the original subject, but may serve other equally



valuable purposes. Truths built on observation and experience, seldom stand single; they generally lead to others, and become the means of more diffusive knowledge.

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The Disease, of which I am to speak, is a disease of the Spine, producing an alteration in its natural figure, and not unfrequently attended with a partial, or a total loss of the power of using, or even of moving, the lower limbs.

From this last circumstance, (the loss of the use the limbs) it has in general been called a Palsy, and treated as a paralytic affection; to which it is in almost every respect perfectly unlike.

The occasion of the mistake is palpable; the patient is deprived of the use of his legs, and has a deformed incurvation of the Spine; the incurvation is supposed to be caused by a dislocation of the vertebrae; the displaced bones are thought to make an unnatural pressure on the spinal marrow, and a pressure on that being very likely to produce a paralysis of some kind, the loss of the use of the legs is in this case determined to be such: the truth is, that there is no dislocation, no unnatural pressure made on the spinal marrow, nor are the limbs by any means paralytic, as will appear to whoever will examine the two complaints with any degree of attention.

In the true paralysis, from whatever cause, the muscles of the affected limb are soft, flabby, unresisting, and incapable of being put into even a tonic state; the limb itself may be placed in almost any position or posture; if it be lifted up, and then let go, it falls down, and it is not in the power of the patient to prevent, or even to retard its fall: the joints are perfectly and easily moveable in any direction; if the affection be of the lower limbs, neither hips, knees, nor ankles, have any degree of rigidity or stiffness, but permit the limb to be turned or twisted in almost any manner.

In the present case, the muscles are indeed extenuated, and lessened in size; but they are rigid, and always at least in a tonic state, by which the knees and ankles acquire a stiffness not very easy to overcome; by means of this stiffness, mixed with a kind of spasm, the legs of the patient are either constantly kept stretched out strait, in which case considerable force is required to

bend the knees, or they are by the action of the stronger muscles drawn across each other, in such manner as to require as much to separate them: when the leg is in a strait position, the extensor muscles act so powerfully as to require a considerable degree of force to bend the joints of the knees; and when they have been bent, the legs are immediately and strongly drawn up, with the heels toward the buttocks: by the rigidity of the ankle joints, joined to the spasmodic action of the gastrocnimii muscles, the patient's toes are pointed downward in such manner as to render it impossible for him to put his foot flat to the ground; which makes one of the decisive characteristics of the distemper.

These are strong marks of the distinction which ought to be made between the two diseases; and fully sufficient to show the impropriety of confounding them with each other.

The majority of those who labor under this disease are infants or young children: Adults are by no means exempt from it, but I have never seen it at an age beyond forty.

When it attacks a child who is old enough to have walked properly, its awkward and imperfect manner of using its legs, is the circumstance which first excites attention, and the incapacity of using them at all, which very soon follows, fixes that attention, and alarms the friends.

The account most frequently given is, that for some time previous to the incapacity, the child had been observed to be languid, listless, and very soon tired; that he was unwilling to move much, or briskly; that he had been observed frequently to trip and stumble, although no impediment lay in his way; that that when he moved hastily or unguardedly, his legs would cross each other involuntarily, by which he was often and suddenly thrown down; that if he endeavoured to stand still, and upright, unsupported by another person, his knees would totter and bend under him; that he could not with any degree of precision or certainty, steadily direct either of his feet to any particular point, but that in attempting so to do, they would be suddenly, and involuntarily brought across each other; that soon after this, he complained of frequent pains and twitchings in his thighs, particularly when in bed, and of an uneasy sensation at the pit

of his stomach; that when he sat on a chair, or a stool, his legs were almost always found across each other, and drawn up under the seat; and that in a little time after these particulars had been observed, he totally lost the power of walking.

These are the general circumstances which are found, at least in some degree, and that pretty uniformly in most infants and children, but there are others which are different in different subjects.

If the incurvation be of the neck, and to a considerable degree, by affecting several vertebrae, the child finds it inconvenient and painful to support its own head, and is always desirous of laying it on a table or pillow, or any thing to take off the weight. If the affection be of the dorsal vertebrae, the general marks of a distempered habit, such as loss of appetite, hard dry cough, laborious respiration, quick pulse, and disposition to hectic, appear pretty early, and in such a manner as to demand attention: and as in this state of the case there is always, from the connection between the ribs sternum and spine a great degree of crookedness of the trunk, these complaints are by every body set to the account of the deformity merely. In an adult, the attack and the progress of the disease are much the same, but there are some few circumstances which may be learned from a patient of such age, which either do not make an impression on a child, or do not happen to it.

An adult, in a case where no violence hath been committed, or received, will tell you, that his first intimation was a sense of weakness in his back bone, accompanied with what he will call a heavy dull kind of pain, attended with such a lassitude as rendered a small degree of exercise fatiguing: that this was soon followed by an unusual sense of coldness in his thighs, not accountable for from the weather, and a palpable diminution of their sensibility. That in a little time more, his limbs were frequently convulsed by involuntary twitchings, particularly troublesome in the night: that soon after this, he not only became incapable of walking, but that his power either of retaining or discharging his urine and faeces was considerably impaired, and his penis became incapable of erection.

The adult also finds all the offices of his digestive, and respiratory organs much affected, and complains constantly of pain and tightness at his stomach.

In infants, the curve is seldom noticed till it has got to such size and state, as to demand attention from the deformity: previous to this, all the marks of distemper which appear in the child, pass for the effects of general weakness, and are treated as such; differently by different people, and under different circumstances, but never with any permanent good effect; some of the adventitious symptoms if I may so call them, are, in some degree relieved, but the principal remain in full force, or what is much more frequent, go on increasing.

In an adult it passes for rheumatism, or gravel, or a strain, and the defect in the limbs is the first thing that occasions an inquiry into the state of the back bone.

When a curvature is perceived in an infant, it is always supposed to have received a hurt by a blow, or fall, and an adult has always recourse to some exertion in pulling, drawing, lifting, or carrying, by which the spine is thought to have been deranged, or injured; but which supposition is seldom, if ever true in either case.

The true cause of the disease, is a morbid state of the spine, and of some of the parts connected with it; which distempered state of parts will upon careful inquiry, be always found to have preceded the deformity some length of time; in infants this is the sole cause, and external violence has nothing to do with it. In the adult, I will not assert that external mischief is always and totally out of the question, but I will venture to affirm what is equal, as far as regards the true nature of the case, which is, that although accident and violence may in some few instances be allowed to have contributed to its more immediate appearance, yet the part in which it shows itself, must have been previously in a morbid state, and thereby predisposed for the production of it. I do not by this mean to say that a violent exertion can not injure the spine, nor produce a paralytic complaint, that would be to say more than I know; but I will venture to assert, that no degree of violence whatever is capable of producing such

The same failure of success attends the use of the different pieces of machinery, and for reasons which are equally obvious.

They are all, from the most simple to the most complex, but particularly the swing and the screw, calculated to obviate and remove what does not exist. They are founded upon the supposition of an actual *dislocation* which never is the case, and therefore they always have been and ever must be unsuccessful.

To understand this in the clearest and most convincing manner, we need only reflect on the nature of the disease, its seat, and the state in which the parts concerned must necessarily be.

The bones are either already carious, or tending to become so; the parts connected with them are diseased, and not infrequently ulcerated; there is no displacement of the vertebrae with regard to each other, and the spine bends forward only because the rotten bone, or bones intervening between the sound ones give way, being unable in such state to bear the weight of the parts above. The most superficial reflection on this must point out to every one, why attempts of this kind can do no good, and a little more attention to the subject will shew why they may be productive of real, and great mischief. The bones are supposed to be sound, but displaced; these machines are designed to bring them back to their former situation, and thereby to restore to the spine its proper rectitude; if therefore they have any power, that power must be exercised on the parts in connection with the curve; which parts, when the disease is at all advanced, are incapable of bearing such a degree of violence without being much hurt thereby: this, if it were merely theoretical, being a conclusion drawn from the obvious and demonstrable state of the distempered parts, could not be deemed unreasonable; but, unfortunately for the afflicted, it is confirmed by practice. They who have had patience and fortitude to bear the use of them to such a degree as to affect the parts concerned, have always found increase of pain and fever, and an exasperation of all their bad symptoms, and I have known more than one instance in which the attempt has proved *fatal*.

The use of some or other of these pieces of machinery is so general, and the vulgar prejudice in their favour so great, that

notwithstanding I have been long convinced of their perfect inutility, yet if I had no other objection to them, I would not attempt to rob the afflicted of what they seem to derive such comfortable expectation from; but as I am satisfied of their mischievous effects, not only in the case of the present subject, but in many others; I can not help bearing my testimony against the indiscriminate and very improper use which is daily made of them.

They are used with design to prevent growing children from becoming crooked or mishapen, and this they are supposed to do by supporting the back-bone, and by forcing the shoulders unnaturally backward; the former they can not do, and in all cases where the spine is weak, and thereby inclined to deviate from a right figure, the latter action of these instruments must contribute to rather than prevent such deviation; as will appear to whoever will with any attention examine the matter: if, instead of adding to the embarrassments of childrens dress by such iron restraints, parents would throw off all of every kind, and thereby give nature an opportunity of exerting her own powers; and if in all cases of manifest debility recourse was had to friction, bark, and cold bathing, with a due attention to air, diet, exercise, and rest, the children of the opulent would, perhaps, stand a chance of being as stout, as strait, and as well shapen as those of the laborious poor.

When a child appears to be what the common people call naturally weakly, whatever complaints it may have are supposed to be caused by its weak state, and it is generally believed that time and common care will remove them; but when a curvature has made its appearance, all these marks of ill health, such as laborious respiration, hard cough, quick pulse, hectic heat and flushing, pain and tightness of the stomach, &c. are more attentively regarded, and set to the account of the deformity consequent to the curve, more especially if the curvature be of the dorsal vertebrae, in which case the deformity is always greatest: but whoever will carefully attend to all the circumstances of this disorder, will be convinced, that most, if not all the complaints of children, labouring under this infirmity, precede the curvature,

and that a morbid state of the spine, and of the parts connected with it, is the original and primary cause of both.\*

I have in the former edition informed the reader, that my particular attention to this disease was first excited by an instance of its being cured by a seemingly accidental abscess; that this first gave me reason to suspect, that we had mistaken an effect for a cause, and, that upon mature deliberation upon the matter, I was still more inclined to think so for the following reasons.

1. "That I did not remember ever to have seen this useless state of the limbs from a mere malformation of the spine, however crooked such malformation might have made it.

2. "That none of these deviations from right shape, which growing girls are so liable, to however great the deformity might be, was ever attended with this effect.

3. "That the kind of deformity, which was attended with this affection of the limbs, although it was different as to its degree, and its extent in different people, yet it was uniform in one circumstance, which was, that the curvature always was from within outwards.

4. "That since I had been particularly attentive to the disorder, I thought that I had observed, that neither the extent, nor degree of the curve, had in general produced any material difference in the symptoms, but that the smallest was, when perfectly formed, attended with the same consequences as the largest."

5. That although it had sometimes happened, that a blow, or a strain, had preceded the appearance of the curve, yet it much more frequently happened, that no such cause was assignable.

6. "That I had observed exactly the same symptoms in infants, and in young children, who had neither exerted themselves, nor

\* "When I published the first edition of this tract, I was not so aware of this truth, as a more enlarged experience in, and a more careful attention to the disorder since has made me.

"I am very glad to embrace this opportunity of acknowledging, and of correcting the mistake, and the more for as I am convinced that an inference of the greatest importance may be drawn from it. I am satisfied that this malady may, in many instances, by early and proper attention, be prevented from producing its otherwise inevitable consequences, temporary lameness, and permanent deformity."

were supposed to have received any injury from others; and that the case was still the same in those adults, who had no such cause to look to."

7. That although it might be expected, that a dislocation of any of the vertebrae, would be attended with symptoms of the paralytic kind, yet they would be very unlike to those which affected the limbs in the present case.

The suspicions which these circumstances had excited in my mind, were confirmed\* by what I had a few opportunities of observing, in the dead bodies of some who had died afflicted with this disorder, and altogether satisfied me, that there must be something predisposing in the parts concerned; and that when we attribute the useless state of the limbs merely to the curvature, we mistake, as I have just said, an effect for a cause.

At the same time I gave an account of a conversation, which passed between me and the late Dr. Cameron, of Worcester, who told me, that having remarked in Hippocrates, an account of a paralysis of the lower limbs, cured by an abscess in the back he had in a case of useless limbs attended, with a curvature of the spine, endeavoured to imitate this act of nature by exciting a purulent discharge, and that it had proved very beneficial, which was confirmed to me by Mr. Jeffries, of Worcester, who had made the same experiment with the same success.†

From the time of my receiving this first information to the present, I have sought every opportunity of making the experi-

\* In the first edition I had described the bones on which the disease had seized, as being enlarged and spread; upon repeated inquiry and examination, I am convinced that they are not.

The bodies of the vertebrae concerned are often affected, while the ligaments bear but little mark of distemper; but whether the ligaments be affected, or not, the bodies of the vertebrae are always diseased, which disease does not so properly *enlarge as erode*, the state also of the intervertebral cartilages, I find to be subject to great variety, they being sometimes totally destroyed, while the caries is small in degree, sometimes apparently but little injured, where the caries has done considerable mischief, and sometimes totally destroyed and annihilated.

† In this place of the first edition, I gave a short account of the first two or three cases which occurred to me; in this I omit them as needless.

The number of experiments which have been made by many of the most eminent practitioners, at home and abroad, have sufficiently established the fact, and render the relation of particular cases unnecessary.



ment; St. Bartholomew's Hospital has seldom been without cases of this kind, and it is with infinite pleasure and satisfaction, that I find myself enabled to say, that in all cases where the complaint has been so circumstanced as to admit of even probable expectation, the attempt has been successful.

If the cure of this most dreadful distemper had depended upon an application to the constitution in general, it might have required a variety of medicines, the administration of which must have demanded judgment in adapting them to particular persons and constitutions; and it must also, in the nature of things, have happened that many individuals could not have been benefited at all. But fortunately for the afflicted, the means of relief are simple, uniform, and safely applicable to every individual, under almost every possible circumstance, not attended by the smallest degree of hazard, and capable of being executed by any body who has the least portion of chirurgic knowledge: it consists merely in procuring a large discharge of matter, from underneath the *membrana adiposa* on each side of the distempered bones forming the curvature, and in maintaining such discharge until the patient shall have recovered his health and limbs. They who are little conversant with matters of this sort, will suppose the means very inadequate to the proposed end; but they who have been experimentally acquainted with the very wonderful effects of purulent drains, made from the immediate neighbourhood of diseases, will not be so much surprised at this particular one; and will immediately see how such kind of discharge, made, and continued from the distempered part, checks the further progress of the caries, give nature an opportunity of exerting her own powers of throwing off the diseased parts, and of producing by incarnation an union of the bones (now rendered sound) and thereby establishing a cure.

However, be all this as it may, the fact is undoubted, and the number of witnesses, as well as patients producible in confirmation of it is so considerable, that it is needless to say any thing more on that head.

It is a matter of very little importance towards the cure, by what means the discharge be procured, provided it be large, that

it come from a sufficient depth, and, that it be continued for a sufficient length of time.\*

I have tried the different means of setons, issues by incision, and issues by caustic, and have found the last in general preferable, being least painful, most cleanly, most easily manageable, and capable of being longest continued.

The caustics should be applied on each side of the curvature, in such a manner as to leave the portion of skin covering the spinal processes of the protruding bones, entire and unhurt, and so large, that the sores upon the separation of the eschars, may easily hold each three or four peas in the case of the smallest curvature; but in large curves, at least as many more.

These issues should not only be kept open, but the discharge from them should be maintained by means of orange peas, cantharides in fine powder, *aerugo aeris*, or any such application as may best serve the intended purpose, which should be that of a large, and long continued drain.

Whatever length of time it may take to obtain a complete cure, by restoring the health as well as the limbs, the issues must be continued at least as long; and in my opinion, a considerable time longer, especially in the persons of infants and growing children; the necessity of which will appear more strongly, when it shall be considered that infants and young children of strumous habits, are the subjects who are most liable to this distemper, and that in all the time previous to menstruation in one sex, and puberty in the other, they are in general more served by artificial drains than any other persons whatever.

This, and this only, does or can alleviate the misery attending this distemper, and in proper time effect a cure.

By means of these discharges, the eroding caries is first checked, and then stopped; in consequence of which an incarnation takes place, and the cartilages between the bodies of the vertebrae having been previously destroyed, the bones become united with each other and form a kind of ankylosis.

The time necessary for the accomplishment of this, must, in the

\* When I say this, I mean to signify that it is absolutely without limitation, and must depend on their beneficial effect.

nature of things, be considerable in all cases, but very different according to different circumstances.

No degree of benefit or relief, nor any the smallest tendency towards a cure is to be expected, until the caries be stopped, and the rotten bones have begun to incarn; the larger the quantity of bones concerned, and the greater degree of waste and havock committed by the caries, the greater must be the length of time required for the correction of it, and for restoring to a sound state so large a quantity of distempered parts.—and vice versa.\*

In the progress toward a cure, the same gradation or succession of circumstances may be observed, as was found to attend the formation of the disease, with this difference, that they which attend the latter, are much more rapid than those which accompany the former.

After the discharge has been made some time, very uncertain that the patient is found to be better in all general respects, and if of age to distinguish, will acknowledge that he feels himself to be in better health; he begins to recover his appetite, gets refreshing sleep, and has a more quiet and less hectic kind of pulse, but the relief which he feels above all others, is from having got rid of that distressing sensation of tightness about the stomach, in a little time more a degree of warmth, and a sensibility is felt in the thighs, which they had been strangers to for some time, and generally much about the same time, the power of retaining and discharging the urine and feces begins to be in some degree exerted.

The first return of the power of motion in the limbs is rather disagreeable, the motions being involuntary and of the spasmodic kind, principally in the night; and generally attended with a sense of pain in all the muscles concerned.

At this point of amendment, if it may be so called, it is no uncommon thing, especially in bad cases, for the patient to stand sometime without making any farther progress; this in adults occasions impatience, and in parents despair; but in the milder

\* Nothing can be more uncertain than the time required for the cure of this distemper. I have seen it perfected in two or three months, and I have known it require two years; two-thirds of which time passed before there was any visible amendment.

kind of case, the power of voluntary motion generally soon follows the involuntary.

The knees and ankles by degrees lose their stiffness, and the relaxation of the latter enables the patient to set his feet flat upon the ground, the certain mark that the power of walking will soon follow; but those joints having lost their rigidity become exceedingly weak, and are not for some time capable of serving the purpose of progression.

The first voluntary motions are weak, not constantly performable, nor even every day, and liable to great variation, from a number of accidental circumstances, both external and internal.

The first attempts to walk are feeble, irregular, and unsteady, and bear every mark of nervous, and muscular debility; the patient stands in need of much help, and his steps, with the best support, will be, as I have just said, irregular and unsteady; but when they have arrived at this, I have never seen an instance in which they did not soon attain the full power of walking.

When the patient can just walk, either with crutches, or between two supporters, he generally finds much trouble and inconvenience, in not being able to resist, or to regulate, the more powerful action of the stronger muscles of the thigh over the weaker, by which his legs are frequently brought involuntarily across each other, and he is suddenly thrown down.

Adults find assistance in crutches, by laying hold of chairs, tables, &c. but the best and safest assistance for a child, is what is called a go-cart, of such height as to reach under the arms, and so made as to enclose the whole body: this takes all inconvenient weight off from the legs, and at the same time enables the child to move them as much as it may please.

Time and patience are very requisite; but they do in this case, as in many others, accomplish our wishes at last.

The deformity remaining after recovery is subject to great uncertainty, and considerable variety, as it depends on the degree of caries, and the number of bones affected: in general, it may be said, that where one vertebrae only is affected, and the patient young, the curve will in length of time almost totally disappear; but where two or three are affected, this cannot be expected;

the thing aimed at is the consolidation and union of the bones, which had been carious, and are now become sound: this is the *sine qua non* of the cure, and this must in such cases render the curvature, and consequently the deformity, permanent: the issues will restore the use of the limbs, but not the lost figure of the spine.

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Since this method of treating the distemper has been made known, the disease itself has been more adverted to, and applications for relief have been more frequent than they were while it was regarded as incurable. The number received into St. Bartholomew's Hospital, has been considerable, and, as it may be supposed, some in a state to admit of cure, others not. While the thing was new, and before a number of cures sufficient to establish the fact had been wrought, it was doubted by most, and positively denied by some; but since a variety of successes has put the matter beyond all doubt, with regard to the restoration of the use of the limbs, it has been said, that as the disease is manifestly a disease of the bones, it is to be apprehended, that the expectation of relief may in some cases fail, and that in others it may not prove permanent; that the same kind of constitution remaining, a return of the malady may be feared; and, in short, that a much greater degree of uncertainty may occur, than might be expected from the account which I have given.

To the first I answer, that in cases where the caries is very extensive, and the constitution has been thereby so injured as to produce a degree of mischief tending to the destruction of the patient, no good is to be expected; the disease has been too long neglected, and is become thereby an overmatch for the remedy. But how does this differ from what may be said, with the same truth, of every disease, and of every remedy. To the second, third, and fourth remark, all I can say is, that in the space of three years, during which I have had many opportunities of making the experiment, I have met with but one single instance in which it has failed, where, from the state of the disease, and of the patient, there was any reasonable foundation for hopes; that all those who have submitted to keep the issues open long enough, have been so

restored to health, and to the free use of their limbs, as to be perfectly capable, not only of exercise, but of hard labour, and that I have never yet, among those so treated, met with one on whom the disease has returned

On the other hand, the nature of the original distemper in the habit, its effects both local and general, the gradual, slow manner in which alone a cure is obtainable, and the particular circumstance on which such cure entirely depends, I mean the removal of the caries, and the union of the bones with each other, all very strongly point out the propriety of continuing that discharge for a sufficient length of time, from which, and from which only, such benefit has been derived.

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At the beginning of the preceding tract I have said, that when I first began to consider the distemper with that degree of attention which it seemed to deserve, I was inclined to suspect that we had hitherto regarded it too superficially; that we had been satisfied with observing its external appearance merely, without enquiring into its real nature; that we had thereby been led to mistake an effect for a cause, and that there must certainly be either in the constitution of the patient, or in the state of the parts concerned, something which tended to produce this very dreadful malady.

I am satisfied I was right in my conjecture, and am convinced, from every circumstance, general and particular, in the living, and from every appearance in the dead, that the complaint arises from what is commonly called a strumous, or scrophulous indisposition, affecting the parts composing the spine, or those in its immediate vicinity.

This morbid affection shows itself in a variety of forms, but, although its appearances be various, yet they are always such as determine the true nature of the distemper.

Sometimes it appears in a thickened state of the ligaments, connecting the vertebrae together, without any apparent affection of the bones.

Sometimes in the form of a distempered state of the intervertebral substances, called cartilages.

Sometimes in that of diseased glands, either in a merely in-

durated and enlarged state, or what is more frequent, in that of a partial suppuration.

Sometimes it is found in the form of bags or cysts, containing a quantity of stuff of a very unequal consistence, partly purulent, partly sanious, and partly a curd-like kind of substance; and not unfrequently entirely of the last.

Sometimes under these bags, or cysts, even while they remain whole, the subjacent bones are found to be distempered, that is, deprived of periostium, and tending to become carious.

Sometimes these collections erode the containing membranes, and make their way downward by the side of the psoas muscle, toward the groin, or by the side of the pelvis behind the great trochanter, or in some cases to the outside of the upper part of the thigh.

Sometimes each of the distempered states of these parts is accompanied by a greater or less degree of deformity, and crookedness of the spine without any apparent disease of the bones composing it: sometimes the deformity is attended with an erosion, or caries of the body or bodies of some of the vertebrae; and sometimes the same bones are found to be carious, without any crookedness or alteration of figure.

These different affections of the spine, and of the parts in its immediate neighbourhood, are productive of many disorders, general and local, affecting the whole frame and habit of the patient, as well as particular parts; and among the rest, of that curvature which is the subject of this enquiry; and it may not be amiss to remark, that strumous tubercles in the lungs, and a distempered state of some of the abdominal viscera, often make a part of them.

From an attentive examination of these morbid appearances, and of their effects in different subjects, and under different circumstances, the following observations, sending not only to illustrate and explane the true nature of the disease in question, but also to throw light on others of equal importance, may I think be made.

1. That the disease which produces these effects on the spine, and the parts in its vicinity, is what is in general called the scrophula; that is, that same kind of indisposition as occasions

the thick upper lip, the tedious obstinate ophthalmy, the indurated glands under the chin, and in the neck, the obstructed mesentary, the hard dry cough, the glairy swellings of the wrist and ancles, the thickened ligaments of the joints, the enlargement, and caries of the bones, &c. &c. &c.

2. That this disease, by falling on the spine, and the parts connected with it, is the cause of a great variety of complaints, both general and local.

3. That when these complaints are not attended with an alteration of the figure of the back bone, neither the real seat, nor true nature of such distemper are pointed out by the general symptoms, and consequently, that they frequently are unknown, at least while the patient lives.

4. That when by means of this distemper an alteration is produced in the figure of the back bone, that alteration is different in different subjects, and according to different circumstances.

5. That when the ligaments and cartilages of the spine become the seat of the disorder, without any affection of the vertebrae, it sometimes happens that the whole spine, from the lowest vertebra of the neck downwards, gives way laterally, forming sometimes one great curve to one side, and sometimes a more irregular figure, producing general crookedness and deformity of the whole trunk of the body, attended with many marks of ill health.

6. That these complaints, which are by almost every body supposed to be the effect of the deformity merely, are really occasioned by that distempered state of the parts within the thorax, which is at the same time the cause both of the deformity and of the want of health.

7. That the attack is sometimes on the bodies of some of the vertebrae; and that when this is the case, ulceration or erosion of the bone, is the consequence, and not enlargement.

8. That when this erosion or caries seizes the body or bodies of one or more of the vertebrae, it sometimes happens that the particular kind of curvature which makes the subject of these sheets is the consequence.

9. That this curvature, which is always from within outward,



is caused by the erosion or destruction of part of the body or bodies of one or more of the vertebrae; by which means that immediately above the distemper, and that immediately below it, are brought nearer to each other than they should be, the body of the patient bends forward, the spine is curved from within outward, and the tuberosity appears behind, occasioned by the protrusion of the spinal processes of the distempered vertebrae. See plate 1, 2, and 3.

10. That according to the degree of carious erosion, and according to the number of vertebrae affected, the curve must be less or greater.

11. That when the attack is made upon the dorsal vertebrae, the sternum and ribs, for want of proper support, necessarily give way, and other deformity, additional to the curve is thereby produced.

12. That this kind of caries is always confined to the bodies of the vertebrae, seldom or never affecting the articular processes.\*

13. That without this erosive destruction of the bodies of the vertebrae, there can be no curvature of the kind which I am speaking of; or, in other words, that erosion is the *sine qua non* of this disease; that although there can be no true curve without caries, yet there is, and that not infrequently, caries without curve. See plate 5.

14. That the caries with curvature and useless limbs, is most frequently of the cervical or dorsal vertebrae; the caries without curve, of the lumbal, though this is by no means constant or necessary.

15. That in the case of carious spine, without curvature, it most frequently happens, that internal abscesses, and collections of matter are formed, which matter makes its way outward, and appears in the hip, groin, or thigh; or, being detained within the body, destroys the patient: the real and immediate cause of whose death is seldom known, or even rightly guessed at, unless the dead body be examined.

\*I have seen two cases in which the bodies of the vertebrae were totally separated from all connection with the other parts, leaving the membrane, which included the spinal marrow, perfectly bare. See plate 4.

16. That what are commonly called lumbal and psoas abscesses, are not infrequently produced in this manner, and therefore when we use these terms, we should be understood to mean only a description of the course which such matter has pursued in its way outward, or the place where it makes its appearance externally, the terms really meaning nothing more, nor conveying any precise idea of the nature, seat, or origin of a distemper subject to great variety, and from which variety its very different symptoms and events, in different subjects, can alone be accounted for.

17. That contrary to the general opinion, a caries of the spine is more frequently a cause than an effect of these abscesses.

18. That the true curvature of the spine, from within outward, of which the paralytic, or useless state of the lower limbs, is a too frequent consequence, is itself but *one* effect of a distempered spine; such case being always attended with a number of complaints which arise from the same cause: the generally received opinion, therefore, that all the attending symptoms are derived from the curvature, considered abstractedly, is by no means founded in truth, and may be productive of very erroneous conduct.

19. That in the case of true curvature, attended with useless limbs, there never is a *dislocation*, properly to be so called; but that the alteration in the figure of the back bone, is caused solely by the erosion and destruction of a part of one or more of the corpora vertebrarum; and, that as there can be no true curvature without caries, it must be demonstrably clear, that there must have been a distempered state of parts previous to such erosion; from all which it follows, that this distemper, call it by what name you please, ought to be regarded as the original cause of the whole, that is, of the caries, of the curvature, and all the attendant mischiefs, be they what they may, general or particular: a consideration, as it appears to me, of infinite importance to all such infants and young children, as shew either from their general complaints, or from their shape, a tendency to this kind of evil; and whose parents and friends generally content themselves with a swing, or piece of iron machinery, and look no farther.

20. That whoever will consider the real state of the parts when

a caries has taken place, and the parts surrounding it are in a state of ulceration, must see why none of the attempts, by means of swings, screws, &c. can possibly do any good, but, on the contrary, if they act so as to produce any effect at all, it must be a bad one.

21. That the discharge, by means of the issues, produces in due time (more or less under different circumstances) a cessation of the erosion of the bones; that this is followed by an incarnation, by means of which the bodies of the vertebrae which had been the seat of the disease, coalesce, and unite with each other, forming a kind of anchylosis.

22. That the different degrees and extent of the caries, in different subjects, must render all attempts to cure uncertain, both as to the time required, and as to the ultimate event: the least and smallest degree will (every thing else being equal) be soonest relieved and cured; the larger and more extensive will require more time, and where the rottenness is to a great degree, and all the surrounding parts in a state of distempered ulceration, it must foil all attempts, and destroy the patient.

23. That when two or more vertebrae are affected, forming a large curve, however perfect the success may be with regard to the restoration of health and limbs, yet the curvature will and must remain, in consequence of the union of the bones with each other.

24. That the useless state of the limbs is by no means a consequence of the altered figure of the spine, or of the disposition of the bones with regard to each other, but merely of the caries: of this truth there needs no other proof, than what may be drawn from the cure of a large and extensive curvature, in which three or more vertebrae were concerned: in this the deformity always remains unaltered and unalterable, notwithstanding the patient recovers both health and limbs.

Upon the whole, after due consideration of what has been said concerning the nature of the complaint, its producing cause, and the method by which it is capable of being cured, I would ask, whether the diseased state of the spine, and of the parts connected with it, (which, if not prevented, must produce some of its very

dreadful effects,) may not, by a timely use of proper means, be prevented?

A morbid state of parts previous to deformity, caries, or curve, must be allowed: every complaint of the living, and every appearance in the dead, prove it beyond contradiction or doubt. All the general complaints of persons afflicted with this disorder will always, upon careful enquiry, be found to have preceded any degree of deformity, to have increased as the curve became apparent, and to have decreased as the means used for relief took place: the pain and tightness about the stomach, the indigestion, the want of appetite, the disturbed sleep, &c. &c. gradually disappear, and the marks of returning health become observable before the limbs recover the smallest degree of their power of moving.

On the other hand, it is as true, that when from extent, or degree, or inveteracy of the caries, the issues are found to be unequal to the wished-for effect, the general complaints receive no amendment, but increase until the patient sinks under them.

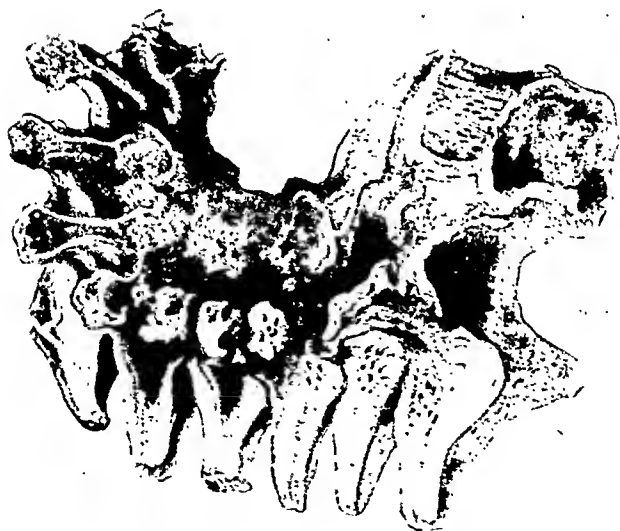
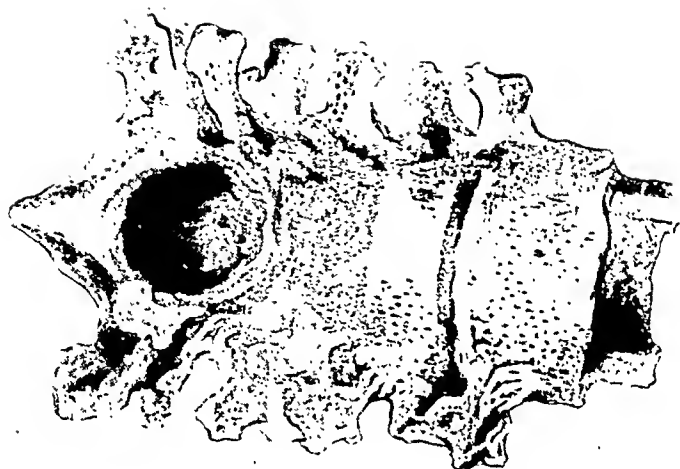
If all this be true, which that it is, the manifold and repeated experience of many, as well as myself, can amply testify; and if it be found that the issues are capable of affecting a perfect curve, even after a caries has taken place, and that to a considerable degree, which is also true to demonstration, is it not reasonable to conclude, that the same means made use of in due time might prove preventive.

If this was a matter of mere speculation, or opinion, I would be very cautious how I spake of the subject; but it is really a matter of experiment; and as far as I have had it in my power to put it to that test, it has succeeded, by the restoration of lost health, and the prevention of a deformity which was advancing rapidly.

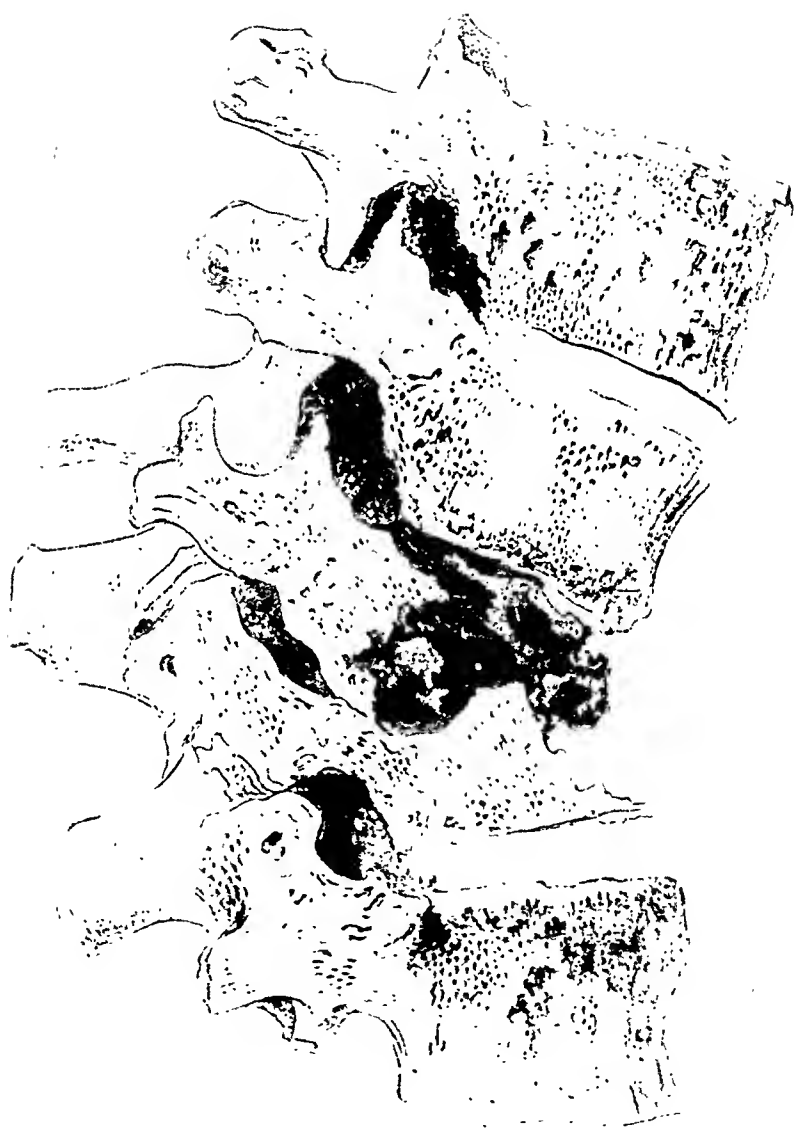
It may, perhaps, be said, that if no such means had been used, the same space of time might have produced the same effect: to this it is impossible to make an answer: I shall, therefore, content myself with having given my opinion, with the circumstances and reasons on which it is founded.

I should be sorry to be misunderstood on this point, or to have

it thought that I meant to say, that every weak or rickety child was necessarily liable to a curved spine; or that issues were to be deemed an infallible remedy for the ills arising from a strumous habit: far be it from me to say either: what I would wish to be understood to mean is, that such kind of habit appears to me to be most apt to produce some of the mischiefs mentioned in this tract: that as a purulent discharge, derived from the neighborhood of the spine, is found, from repeated experience, to be a successful remedy, even after the disease is confirmed by a caries, it seems to me to bid fairer than any thing else, if used in time to become a preventive; and, that as some other kinds of deformity are found to follow attacks of the same kind of constitutional disorder seizing on these parts, and which, though not causing precisely the same effect, are nevertheless attended with the same general symptoms; I cannot help thinking, that it may be well worth while to try whether benefit be not obtainable by the same means, in the one case as in the other; and if the old maxim, "*anceps remedium quam nullum*" be admissible, surely an experiment, which is in its nature perfectly incapable of harm, is worth making.



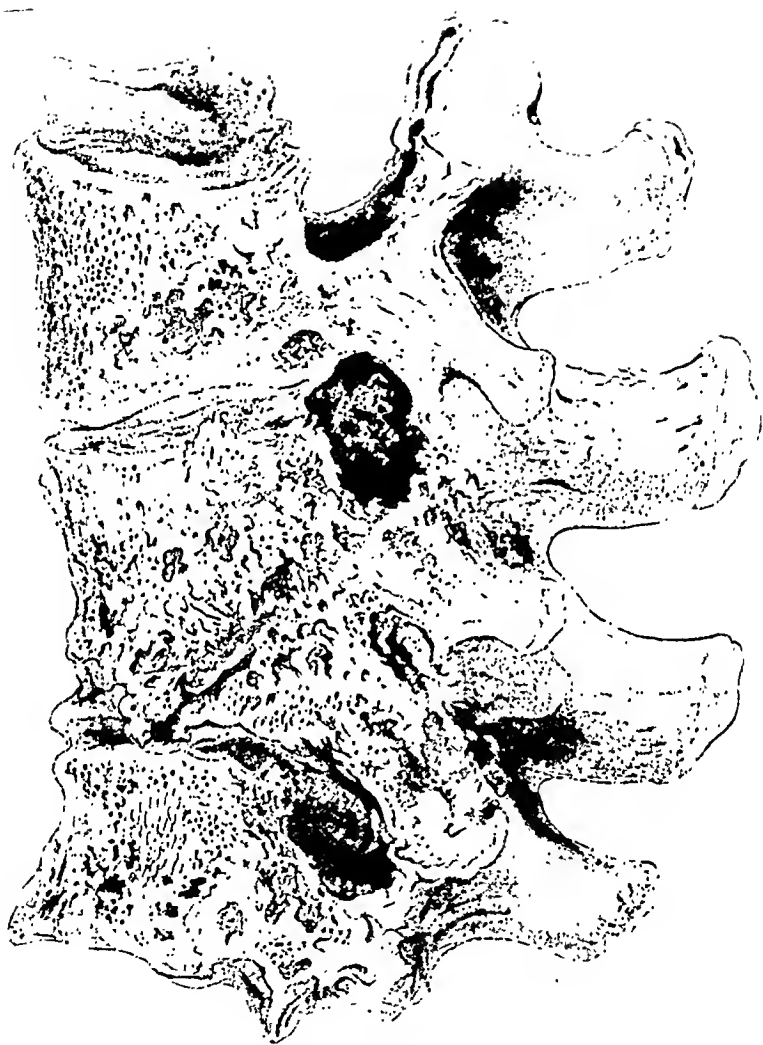












4<sup>th</sup> View of some of the Vertebrae in a case of Curved Spine which had been cured by the Caustic, which were taken from the body of the Patient who died of another distemper at some distance of Time after. In this may be seen the State of the Vertebrae which had been Cured, and of the consequent Ankylosis or Union.

7. *Lawrence, J. V.*

## POTT'S FRACTURE

In 1756 Percivall Pott was thrown from his horse and suffered a compound fracture of the leg, according to the interesting story by Sir James Earle, his son-in-law and biographer. (See Power, Sir D'Arcy in *Brit. J. Surg.*, 10: 313; 433, 1922.) His confinement is supposed to have directed his ambitions to writing but he must have been so inclined before his injury because in the same year he published a work of 232 pages on Ruptures. At any rate there followed in rapid succession a series of important medical books, most of which went through several editions.

There is no evidence that Pott suffered the particular fracture which now bears his name, in spite of many of his biographers; he does mention his own case of compound fracture of the leg with primary union, even though immediate amputation had been advised by several doctors. It seems as though he would have mentioned his own case (if it had existed) of fracture of the fibula and external dislocation of the ankle joint (Pott's fracture). Certainly he stresses the value of recognizing the condition exactly and instituting proper treatment.

Pott's description of this fracture is a classic of medical observation and logic. We can see that he had dissected and carefully studied the anatomy of the ankle region and was able to recognize clearly the altered anatomy even without an x-ray picture to aid (or hinder) his clinical acumen. The entire subject is covered in six and one-half pages of large print, giving the causes of the injury, method of displacement of parts, clinical findings, differential diagnosis, prognosis, treatment and results of improper reduction. Pott's writing is clear, concise, full of common sense and interest, never academic. The article contains a drawing of the characteristic deformity of the ankle and displaced bones which should fix this fracture in the mind of every medical student or doctor.



SOME FEW  
GENERAL REMARKS  
ON  
FRACTURES  
AND  
DISLOCATIONS.

By PERCIVALL POTT, F.R.S.  
AND  
SURGEON to ST. BARTHOLOMEW'S-HOSPITAL.

*Navem agere ignarus navis timet; abrotarum agro  
Non audet, nisi qui didicit dare. Quod medicorum est  
Præmittant medici: tractant familia salvi.*

HORAT.

L O N D O N:

Printed for L. HAWES, W. CLARKE, and R. COLLINS,  
in Pater-noster Row. M.DCC.LXIX.





## Some Few General Remarks on Fractures and Dislocations (Pott's Fracture)

BY

PERCIVALL POTT, F.R.S.

*Surgeon to St. Bartholomew's Hospital*

**L**ET not the reader fancy that I would dare to amuse him with speculation, or merely specious reasoning on a subject like this. What I have said is from experience, repeated experience both of myself and of others, for a considerable length of time past, and on a great variety of subjects; from an experience which has perfectly satisfied me, and I think will every man who will make the trial fairly and candidly. I do not pretend to say, that by these means every kind of broken bone will infallibly and certainly be brought to lie smooth, even, and of proper length; if I did, they who are versed in these things, would know that I said too much; but I will say, (what is sufficient for my purpose) that it will not only succeed in all those, in which the old method can ever be successful, but also in the majority of those in which it is not nor in the nature of things can. In those fortunate cases, in which either method will do, the old one is fatiguing, inconvenient, and even sometimes offensive, from the supine and confined posture of the patient; whereas that which is here proposed gives the patient much greater liberty of motion for every purpose either of choice or necessity, and in many of those cases, wherein the old method proves most frequently so far suc-



cessless, as to leave the limb short, lame, or deformed; I say, in most of these, the proposed method will not be attended with these inconveniences.

I have already said, that in most cases of broken thigh or leg, the method just described will be attended with great success: but there is one particular case in which its utility is still more conspicuous; a case which, according to the general manner of treating it, gives infinite pain and trouble both to the patient and surgeon, and very frequently ends in the lameness and disappointment of the former, and the disgrace and concern of the latter: I mean the fracture of the fibula attended with a dislocation of the tibia.

Whoever will take a view of the leg of a skeleton, will see that although the fibula be a very small and slender bone, and very inconsiderable in strength, when compared with the tibia, yet the support of the lower joint of that limb, (the ankle) depends so much on this slender bone, that without it the body would not be upheld, nor locomotion performed, without hazard of dislocation every moment. The lower extremity of this bone, which descends considerably below that end of the tibia, is by strong and inelastic ligaments firmly connected with the last-named bone, and with the astragalus, or that bone of the tarsus which is principally concerned in forming the joint of the ankle. This lower extremity of the fibula has, in its posterior part, a superficial sulcus for the lodgment and passage of the tendons of the peronei muscles, which are here tied down by strong ligamentous capsulae, and have their action so determined from this point or angle, that the smallest degree of variation from it, in consequence of external force, must necessarily have considerable effect on the motions they are designed to execute, and consequently distort the foot. Let it also be considered, that upon the due and natural state of the joint of the ankle, that is, upon the exact and proper disposition of the tibia and fibula, both with regard to each other and to the astragalus, depend the just disposition and proper action of several other muscles of the foot and toes; such as the gastrocnemii, the tibialis anticus, and posticus, the flexor pollicis longus, and the flexor digitorum pedis longus, as must appear

demonstrably to any man who will first dissect and then attentively consider these parts.

If the tibia and fibula be both broken, they are both generally displaced in such manner, that the inferior extremity, or that connected with the foot, is drawn under that part of the fractured bone which is connected with the knee; making by this means a deformed, unequal tumefaction in the fractured part, and rendering the broken limb shorter than it ought to be, or than its fellow, and this is generally the case, let the fracture be in what part of the leg it may.

If the tibia only be broken, and no act of violence, indiscretion, or inadvertence be committed, either on the part of the patient or of those who conduct him, the limb most commonly preserves its figure and length; the same thing generally happens if the fibula only be broken, in all that part of it, which is superior to letter *A* in the annexed figure, or in any part of it between its upper extremity, and within two or three inches of its lower one.

I have already said, and it will obviously appear to every one who examines it, that the support of the body and the due and proper use and execution of the office of the joint of the ankle depend almost entirely on the perpendicular bearing of the tibia upon the astragalus, and on its firm connection with the fibula. If either of these be perverted or prevented, so that the former bone is forced from its just and perpendicular position on the astragalus, or if it be separated by violence from its connection with the latter, the joint of the ankle will suffer a partial dislocation internally;\* which partial dislocation cannot happen without not only a considerable extension, or perhaps laceration of the bursal ligament of the joint, which is lax and weak, but a laceration of those strong tendinous ligaments, which connect the lower end of the tibia with the astragalus and os calcis, and which constitute in great measure the ligamentous strength of the joint of the ankle.

This is the case, when by leaping or jumping the fibula breaks in the weak part already mentioned, that is within two or three inches of its lower extremity. When this happens, the inferior

\* See the figure on page 332.

fractured end of the fibula falls inward toward the tibia, that extremity of the bone which forms the outer ankle is turned somewhat outward and upward, and the tibia having lost its proper support, and not being of itself capable of steadily preserving its true perpendicular bearing, is forced off from the astragalus inwards, by which means the weak bursal, or common ligament of the joint is violently stretched, if not torn, and the strong ones, which fasten the tibia to the astragalus and os calcis, are always lacerated, thus producing at the same time a perfect fracture and a partial dislocation, to which is sometimes added a wound in the integuments, made by the bone at the inner angle. By this means, and indeed as a necessary consequence, all the tendons which pass behind or under, or are attached to the extremities of the tibia and fibula, or os calcis, have their natural direction and disposition so altered, that instead of performing their appointed actions, they all contribute to the distortion of the foot, and that by turning it outward and upward.

When this accident is accompanied, as it sometimes is, with a wound of the integuments of the inner ankle, and that made by the protrusion of the bone, it not infrequently ends in a fatal gangrene, unless prevented by timely amputation, though I have several times seen it do very well without. But in its most simple state, unaccompanied with any wound, it is extremely troublesome to put to rights, still more so to keep it in order, and unless managed with address and skill, is very frequently productive both of lameness and deformity ever after.

After what has been said, a farther explanation why this is so is unnecessary. Whoever will take even a cursory view of the disposition of the parts, will see that it must be so. By the fracture of the fibula, the dilatation of the bursal ligament of the joint, and the rupture of those which should tie the end of the tibia firmly to the astragalus and os calcis, the perpendicular bearing of the tibia on the astragalus is lost, and the foot becomes distorted; by this distortion the direction and action of all the muscles already recited are so altered, that it becomes (in the usual way of treating this case) a difficult matter to reduce the joint, and, the support of the fibula being gone, a more difficult

one to keep it in its place after reduction. If it be attempted with compress and strict bandage, the consequence often is a very troublesome as well as painful ulceration of the inner ankle, which very ulceration becomes itself a reason why such kind of pressure and bandage can be no longer continued; and if the bone be not kept in its place, the lameness and deformity are such, as to be very fatiguing to the patient, and to oblige him to wear a shoe with an iron, or a laced buskin, or something of that sort, for a great while, or perhaps for life.

All this trouble, pain, difficulty, and inconvenience, are occasioned by putting and keeping the limb in such position, as necessarily puts the muscles into action, or into a state of resistance, which in this case is the same. This occasions the difficulty in reduction, and the difficulty in keeping it reduced; this distorts the foot, and by pulling it outward and upward makes that deformity, which always accompanies such accident; but if the position of the limb be changed, if by laying it on its outside with the knee moderately bent, the muscles forming the calf of the leg, and those which pass behind the fibula and under the os calcis, are all put into a state of relaxation and non-resistance, all this difficulty and trouble do in general vanish immediately; the foot may easily be placed right, the joint reduced, and by maintaining the same disposition of the limb, every thing will in general succeed very happily, as I have many times experienced.



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Sincerely yours  
Theobald Smith

# MEDICAL CLASSICS

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## Theobald Smith

### BIOGRAPHY

- 1859 Born July 31, at 54 Alexander Street, Albany, New York, son of Philip and Theresa Kexel Smith. Educated in Albany schools.
- 1877 Age 18. Gained a State scholarship and entered Cornell University. Earned part of living by playing the organ for chapel services.
- 1881 Age 22. Received degree of Ph.B.
- 1883 Age 24. Received degree of M.D. from Albany Medical College and returned to Cornell for graduate work.
- 1884 Age 25. Director of the pathological laboratory in the U. S. Bureau of Animal Industry until 1895.
- 1886 Age 27. Professor of Bacteriology at Columbian (now George Washington) University until 1895.
- 1888 Age 29. Married to Lilian Hilyer Egleston on May 17. Had three children: Dorothea (Dr. Dorothea E. Smith of Bryn Mawr, Pennsylvania); Lilian (Mrs. Robert F. Foerster, of Princeton); and Philip (of Pawling, New York).
- 1889 Age 30. Published *Preliminary Observations on the Micro-Organisms of Texas Fever*.
- 1893 Age 34. Successfully finished experiments on the cause of Texas fever and published *Investigations into the Nature, Causation and Prevention of Texas or Southern Cattle Fever*.
- 1895 Age 36. Member of Massachusetts State Board of Health and Harvard University Faculty until 1915.

- 1901 Age 42. One of the Board of Directors at founding of The Rockefeller Institute for Medical Research.
- 1915 Age 56. Director of the Department of Animal Diseases of The Rockefeller Institute at Princeton until 1929.
- 1924 Age 65. Vice-president of the Board of Directors of The Rockefeller Institute for Medical Research until 1933.
- 1929 Age 70. Emeritus Director of the Department of Animal Diseases of The Rockefeller Institute until 1934.
- 1933 Age 74. On death of Dr. William H. Welch, became President of the Board of Directors of The Rockefeller Institute for Medical Research.
- 1934 Age 75. Died of heart disease December 10, at New York Hospital, New York City.

A member of Delta Upsilon, Phi Beta Kappa, Sigma Xi and Phi Kappa Phi.

Honorary degrees from the leading colleges, including Harvard, Yale, Princeton, the University of Chicago, Washington University, The University of Pennsylvania, Rutgers and the University of Breslau.

A member of the National Academy of Sciences, the American Philosophical Society, the Association of American Physicians, the Association of American Pathologists and Bacteriologists, and a former president of the National Tuberculosis Association and of the International Union against Tuberculosis. He was an honorary member of the Société de Pathologie Exotique, of Paris; the Royal Academy, of Denmark; the Reale Istituto, of Lombardo, Italy; the Swedish Medical Society, the Royal College of Physicians, of Edinburgh, and the French Academy of Sciences. He was a fellow of the American Academy of Arts and Sciences and an honorary fellow of the Society of Tropical Medicine and Hygiene, of London, and of the Pathologists' Society of Great Britain and Ireland.

Received various awards, including the Mary Kingsley, the Kober, the Flattery, the Trudeau, the Holland Society and the Gerhard medals.

Trustee of the Carnegie Institution of Washington.

## EPONYM

PHENOMENON—anaphylaxis. There is no paper by Theobald Smith on this observation but he transmitted his discovery to Paul Ehrlich in an oral communication. Subsequently, Otto, after working in the Serum Institute at Frankfort, published *Das Theobald Smithsche Phänomen der Serumüberempfindlichkeit* in Lenthold-Gedenkschrift, i, Berlin, 1906.

(Smith's papers in the Journal of Medical Research for 1904, which are usually referred to as the source of the phenomenon, do not treat of that subject.)

INTRODUCTION TO THE WRITINGS OF  
THEOBALD SMITH

Imagine any human being writing two hundred and twenty-four medical papers! And then imagine many of these to be of outstanding value and importance, and several to have completely changed man's conception of certain types of disease and disease transmission. This genius is Theobald Smith.

Smith's greatest work was performed in his early thirties. After graduating from the Albany Medical College in 1883, he returned to Cornell University for graduate work but soon moved on to Washington, D. C., to the Bureau of Animal Industry, whose head, Dr. Daniel E. Salmon, had requested Dr. Simon Henry Gage, Professor of Histology and Embryology at Cornell to furnish a trained assistant. Dr. Gage gladly recommended Theobald Smith because "he knew German and French almost as well as English; physics, chemistry and mathematics seemed native to him. Most important of all, he was a born researcher, with a keenness of insight that promised great things. In his work we had found him tireless and possessing the rare quality of honesty that never deceives itself."

Dr. Salmon was searching for a solution to the problems of diseases that were destroying thousands of the live-stock in America every year. On a foundation of the knowledge established by Pasteur and Koch, Theobald Smith was instrumental in determining the causes of swine plague and hog cholera, and

although his work along this line was not perfect and conclusive, it did aid materially in the final solution of the problems.

During those early days in Washington, Dr. Salmon and Dr. Smith published an epoch-making paper in medical knowledge entitled: *On a New Method of Producing Immunity from Contagious Diseases*, in Proceedings of the Biological Society of Washington, 1-3: 29-33, Feb. 22, 1886. This paper furnished the ground work for studies of artificial immunity, especially in diphtheria and tetanus and should be read by every worker in that field. It is not republished here because a large part of the work was probably Dr. Salmon's and space in this number is already crowded by Dr. Smith's papers.

Theobald Smith's most important and famous work was on Texas fever. He began this study, with other members of the Bureau, in 1884, soon after going to Washington, but the solution was not reached and published until 1893, *Investigations into the nature, causation and prevention of southern cattle fever*. It was written in conjunction with F. L. Kilborne and was published in the Eighth and Ninth Annual Reports for the years 1891 and 1892 of the Bureau of Animal Industry, Washington, Government Printing Office, 1893. The entire work is here reproduced with its many illustrations and plates. It is one of the greatest papers in medical history because it shows for the first time how parasites may act as vectors of disease from animal to animal. Before this knowledge man was fighting an unseen, an unknown foe; after Smith's work, man knew where the foe had its existence. "The Texas fever work opened the road to others for the discovery of the way in which insect carriers transmit the germs of malaria, sleeping sickness, yellow fever, typhus fever, spotted fever, and the bubonic plague" (Gage).

In his preliminary report on Texas fever, a paper delivered before the American Public Health Association in Brooklyn and published in *Medical News*, 55: 689-693, December 21, 1889, Theobald Smith reviews the history of that disease. In 1867 Dr. Stiles of New York undoubtedly saw the parasites in the red blood corpuscles but thought them a loss of substance of the cell body because the cells were shrivelled and crenated. In 1868

the postmortem findings in Texas fever had been thoroughly studied. In 1889 V. Babes described a disease having the same characteristics as Texas fever from which he had recovered a diplococcus, but he was unable to cultivate this organism.

Theobald Smith started his work with three possible solutions in mind. 1. Texas fever might be a disease of the liver with destruction of the blood elements due to absorption of bile from that organ. 2. The disease might be due to a germ which is present in the intestinal tract and possesses a ptomaine capable of dissolving red corpuscles when absorbed into the circulation. Stadelmann, as well as Afanassiew of Germany, had produced a disease having the characteristics of Texas fever by feeding dogs doses of toluylene-diamine. 3. Texas fever might be a disease in which some organism living in the blood itself destroys the red corpuscles. In 1886 at the Bureau of Animal Industry, in two spleens removed from cattle dead of Texas fever, there were found "in or on many red corpuscles small round bodies, perhaps  $1\mu$  in diameter, centrally or somewhat excentrally situated, which stain poorly in an aqueous solution of methyl-violet, very well in aniline-water methyl-violet. They then resemble micrococci in size and form. Unstained, they can be seen as mere transparent spaces in the corpuscles" (Smith).

The problem of Texas fever was so serious that the United States Government had secured the assistance of even the greatest of British veterinarians, Dr. John Gamgee, in studying the disease. All these searchers were unsuccessful in finding the true cause but most of them did isolate some organism, all having, according to Theobald Smith, a postmortem history. Careful bacteriological studies of tissue removed from infected cattle immediately after death revealed no organism. Smith concluded that therefore the organism must reside in the blood cell itself and could not be cultivated as the ordinary microorganism of disease. He also prophesied that the solution of the Texas fever problem will "throw a strong light on human malarial diseases."

But for the careful manner in which Theobald Smith attacked the problem and to gain some idea of the vast amount of work which he did, see his complete paper on the following pages.

"It took four years of slavery at the microscope, at autopsy, at watching ticks hatch from the egg . . ."—  
Theobald Smith.

**TUBERCULOSIS.** After the discovery of the tubercle bacillus, all physicians, even the great Robert Koch himself, thought all tuberculosis due to the same organism. Great fear arose as to wholesale infection from cattle.

Theobald Smith showed, by experiments as rigid as those which led to the true etiology of Texas fever, that man may be infected, at times, by the bovine form of tuberculosis. Such an infection is usually in the alimentary tract of children. These experiments were begun in 1894 and were discussed in a preliminary report before the Association of American Physicians in 1896 (Trans., 11: 75-95). In 1898 he published his conclusions in a masterful paper, *A comparative study of bovine tubercle bacilli, and of human bacilli from sputum*. The entire work is reproduced in its entirety in this number of *Medical Classics*. Smith proved that there were two types of tubercle bacilli, the so-called bovine and human forms. These two types are recognizable by their morphology, by growth and reaction in culture media, by changes in virulence and by effect on the experimental animals.

These experiments were so conclusive that even Robert Koch himself said in 1908, "To Theobald Smith of Harvard belongs the credit of having been the first to call attention to certain differences between the tubercle bacilli found in man and in cattle. It was his work which induced me to take up this same study."

Other works of Theobald Smith which would certainly be included here if space permitted are those on toxin and antitoxin of diphtheria and tetanus, on vaccination, on blackhead among turkeys, several papers on bacteriological technique, especially on the fermentation tube, on colostrum, on *B. abortus*, on streptococci in milk, on medical education, research and scholarship. But the reader must refer to the bibliography of Smith's writings (which see) to appreciate the varied interests and the vast amount of work of this great benefactor of mankind.

## THE THEOBALD SMITH MEMORIAL LABORATORY

In February 1936, the Albany Medical College will dedicate a new teaching and experimental laboratory on the college grounds. This building will house the departments of pharmacology, physiology and experimental surgery and has been appropriately named The Theobald Smith Memorial Laboratory.

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# Investigations into the Nature, Causation, and Prevention of Southern Cattle Fever

BY

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## HISTORICAL REVIEW

**A** CERTAIN number of very important facts had already been ascertained and repeatedly confirmed concerning the nature of Texas or Southern cattle fever up to the time at which these investigations were begun. There were also a number of theories in the field concerning the causation or etiology of this disease, based in part on investigation, in part on speculation.

Of those definitely ascertained facts, we may mention as the most important the one which traced the distribution of the infection to cattle brought from a large but well-defined territory, including most of the Southern States, into more northerly regions. The Southern cattle bearing the infection were, as a rule, free from any signs of disease. It was likewise settled that this infection was carried only during the warmer season of the year, and that in the depth of winter Southern cattle were harmless. It was also known that the infection was not communicated directly from Southern to Northern cattle, but that the ground

over which the former passed was infected by them, and that the infection was transmitted thence to susceptible cattle. All that was necessary for the production of disease was the passage of Southern cattle over a given territory and the grazing of Northern cattle over the same or a portion of the same territory during the same season.

It was also discovered that Southern cattle, after remaining for a short time on Northern pastures, lost, in some mysterious way, the power to infect other pastures and were, for the remainder of their stay North, harmless. Again, cattle driven over a considerable distance lost, after a time on their way, the power to infect pastures. When pastures and trails had been passed over by Southern cattle, it was observed that the disease did not appear at once in the Northern cattle grazing on them, but that a certain period of not less than thirty days elapsed before the native cattle began to die. More curious even than these facts was the quite unanimous testimony of stock-owners who had had more or less experience with this disease, that native susceptible animals which had become diseased did not transmit the disease to other natives, and that they were harmless. We shall discuss this statement in detail, in connection with experiments made to test its accuracy.

If we turn our attention to the opposite aspect of this interesting series of facts, which deals with the introduction of Northern cattle (p. 178) into Southern territory, we learn that such cattle may contract Southern cattle fever, and that it is only under considerable risks that Northern cattle can be introduced into what has been called the permanently infected territory.

These interesting facts about a mysterious disease were largely reasoned out by farmers and stock-owners in their trying experience with it, and were well known before 1868, when the disease began to arouse the attention of the Government, owing to its widespread devastations in the Northern States in that year. The historical record of the development of these ideas is therefore very meager. That Southern cattle in a state of health might bring destruction to Northern herds was observed late in the last century by Dr. Mease. A herd of cattle was driven in 1796

from South Carolina into Pennsylvania, where disease broke out in Lancaster County and other places. This disease was directly traced to the Southern herd by Dr. Mease, who made it the subject of an interesting communication and dwelt particularly upon the fact that the cattle bringing the disease were themselves in good health.

In 1868 Texas cattle shipped up the Mississippi River to Cairo and thence by rail into Illinois and Indiana early in June, caused, during the summer of that year, enormous losses of cattle in these States. Moreover, the East began to be aroused because Western cattle infected with the disease had been shipped eastward for beef and were dying of Texas fever on the way, in the New York stock yards, and elsewhere. The question as to the effect of such diseased flesh upon human health was at that time entirely new and caused much uneasiness. The cattle commissioners of New York State and the board of health of New York City made a vigorous effort to check the importation of diseased cattle from the West, and to their efforts we owe much valuable information of this disease. During that year it was investigated by Dr. R. C. Stiles, for the Metropolitan Board of Health, and by John Gamgee and Drs. John S. Billings and Curtis for the National Government. Since then investigations have been made and published by Drs. D. E. Salmon and Detmers, for the United States Department of Agriculture, and by Drs. Frank S. Billings, Paquin, Dinwiddie, and Francis for the experiment stations of certain States. These various reports will be again referred to under the special subjects to which their authors have given more or less attention.

Perhaps the most important and special contribution to the subject since the earlier investigations of 1868 is the determination of the boundary line of the permanently infected district by Dr. D. E. Salmon. From what has already been stated it will be readily understood that this line marks the northern limit of the territory from which cattle may carry the infection into the territory north of this line. On the other hand, to cross this line from north to south obviously places cattle in the position to contract Texas fever under favorable conditions. The in-

vestigations of Dr. Salmon have shown that this permanently infected area does not extend north of the 37th parallel of latitude, excepting along the eastern slope of the country, where it extends half-way between the 38th and 39th parallels. The order of the Secretary of Agriculture, issued February 26, 1892, puts the following States and Territories entirely within the permanently infected area: South Carolina, Georgia, Florida, Alabama, Mississippi, Arkansas, Louisiana, and Indian Territory. The following are crossed by the boundary line, and are therefore not entirely within the infected area: Virginia, North Carolina, Tennessee, Oklahoma, and Texas. The line as at present defined begins (p. 179) at the Atlantic coast, passing westward on the 38th parallel, and follows the lower boundary of Maryland to the Potomac. It then passes westward across Virginia as far as the eastern slope of the Blue Ridge, which it follows in a southwesterly direction through North Carolina, thus exempting the cooler mountainous regions of these two States from permanent infection. It continues in a nearly westerly direction across the southern strip of western North Carolina and the southern portions of Tennessee. Across the Mississippi it follows the northern boundary of Arkansas and that of the Indian and Oklahoma Territories, and finally passes southward through Texas on or near the 100th meridian.

In addition to this work of accurately defining the territorial distribution of the infection, nothing has been done to add materially to the permanently valuable knowledge concerning this malady. Although attempts have been made to discover the cause they were not successful, as we shall be able to show. In 1889 the first systematic experiments were made by the Bureau of Animal Industry, and these were at once fruitful in the discovery by one of us of a peculiar microörganism in the red blood corpuscles which corresponds in every respect with what we should expect as the true cause. At the same time the other showed by field experiments that the cattle tick was somehow necessary to the transmission of the disease. These observations were fully confirmed in 1890. In the fall of the same year it was observed that when young ticks hatched artificially are placed on

cattle there is a sudden extensive loss of red blood corpuscles, accompanied by fever, which could in no way be explained by the simple abstraction of blood. This discovery, at once followed up by additional experiments, brought to light the remarkable fact that Texas fever is caused by putting recently hatched cattle ticks on susceptible cattle. All these results were reconfirmed in the summers of 1891 and 1892.

These investigations have thus far brought to light two important facts: (1) The constant presence of a blood corpuscle-destroying microörganism in Texas fever, and (2) the transmission of the disease from cattle to cattle by the cattle tick. The various experiments and observations which have led to these results are embodied in the following report and appendix.

The subject of Texas cattle fever has been treated of in the following publications, which are referred to in the text by the number prefixed to each title:

- (1) Transactions of the New York State Agricultural Society, 1867, part 2.
- (2) Reports of the Commissioner of Agriculture on the Disease of Cattle in the United States. Washington, 1871. (Reports by Mr. John Gamgee, J. R. Dodge, and Drs. J. S. Billings and Curtis.)
- (3) Contagious Diseases of Animals. Special Report No. 22. (Report by Dr. D. E. Salmon, pp. 98-142.)
- (4) Report of the Commissioner of Agriculture for 1881-'82. (Report by Dr. D. E. Salmon, pp. 300-306.)
- (5) Contagious Diseases of Animals. Washington, 1883. (Report by Dr. D. E. Salmon, pp. 13-44. Report by Dr. J. H. Detmers, pp. 103-145.)
- (6) First Annual Report of the Bureau of Animal Industry, 1884. (Report by Dr. D. E. Salmon, Chief of the Bureau, pp. 214-221.)
- (7) Second Annual Report of the Bureau of Animal Industry, 1885. (Report by Dr. D. E. Salmon, Chief of the Bureau, pp. 247-274.)
- (8) Bulletin of the Agricultural Experiment Station of Nebraska, II, No. 3. (Southern Cattle Plague and Yellow Fever from

the Etiological and Prophylactic Standpoints. By Frank S. Billings.)

- (9) Texas Fever. By Paul Paquin. (Missouri Agricultural College Experiment Station, Bulletin No. 11, May 1890.)
- (10) Third Annual Report of the Arkansas Experiment Station, 1890. (Report by R. R. Dinwiddie, Veterinarian, pp. 28-122.)

(p. 180)

#### THE NATURE OF TEXAS CATTLE FEVER

##### *Period of Incubation*

This term has no very definite significance in this disease, for it is used to designate different things. Thus it has been employed to indicate the period elapsing between the exposure of susceptible cattle to Southern cattle, or upon fields infected by them and the appearance of the disease. If taken in this sense it may vary from ten to ninety days. The great variation here observed is readily explained by the life-history of the cattle tick, with which this period is intimately associated. A discussion is therefore postponed until the life-history of this parasite has been described, and we content ourselves here by simply mentioning the facts as observed.

This term may also be used to signify the time elapsing between the introduction of the infectious agent into the tissues and fluids of the body and the first appearance of disease. This period is ascertainable by inoculation. In the case of subcutaneous and intravenous injection of blood from cattle suffering with Texas fever, the fever temperature appeared within a few days of the inoculation and outward signs of illness were manifest on or even before the sixth day. It is probable, therefore, that multiplication begins at once after the microparasite has been introduced into the body, and when it has attained a sufficient momentum the external symptoms of disease appear. This may be in from six to ten days, depending on the number of microparasites originally introduced, the predisposition and age of the animals, and the season of the year.

## SYMPTOMS

*Acute type*

In our experiments two types of disease have manifested themselves, the acute fatal type and a mild, rather prolonged, usually nonfatal type. As they differ in many respects, they will be considered separately.

The acute disease is the disease of the hot summer months. It appears suddenly, and as a rule at the same time in all animals of a herd which have been exposed to the same infection together. The fever usually precedes the outward symptoms by several days, and animals apparently quite well will show a high rectal temperature ranging from  $105^{\circ}$  to  $108^{\circ}\text{F}$ . The value of the clinical thermometer in thus detecting disease was pointed out by Gamgee and by the Metropolitan Board of Health in 1868. The latter have recorded a temperature of  $109^{\circ}\text{F}$ . (1, p. 1098). A temperature above  $108^{\circ}\text{F}$ . has not been noted in our experiments. A glance at the table in the appendix will show that the normal morning temperature of the cattle in our experiments ranges from  $100.5^{\circ}\text{F}$ . to  $102.5^{\circ}\text{F}$ ., being in general somewhat lower in autumn than in midsummer. The temperature of calves and young animals may rise to  $103^{\circ}\text{F}$ . without being accompanied by any signs of disease.\*

If the temperature of exposed animals be taken once daily, (p. 181) say in the morning, it will be found that at the outset of the disease it will rise within twenty-four hours from the normal to  $104^{\circ}\text{F}$ . or even higher. In the following twenty-four hours it may rise to  $105^{\circ}$  or  $107^{\circ}\text{F}$ . The continued daily record will then show a high temperature until the disease terminates fatally or in recovery. In the former case it may fall from  $2^{\circ}$  to  $4^{\circ}$

\* These figures agree fairly well with those of other observers. "The temperature of healthy cattle ranges from  $37.6^{\circ}$  to  $39.6^{\circ}\text{C}$ . ( $99.7^{\circ}$  to  $103.3^{\circ}\text{F}$ ). In some cases it may be even a trifle higher or lower. In the morning it is usually, but not invariably  $0.2^{\circ}$  to  $0.4^{\circ}\text{C}$ . ( $0.4^{\circ}$  to  $0.7^{\circ}\text{F}$ .) lower than at night. In calves and heifers it is usually somewhat higher than in old cows. . . . The general average from the results obtained by numerous observers is  $38.8^{\circ}\text{C}$ . ( $101.8^{\circ}\text{F}$ )."—Dieckerhoff (*Lehrbuch d. spec. Pathologie und Therapie f. Thierärzte*, II). During very hot weather the evening temperature of cattle more or less exposed to the sun in the pastures of the station has been found to rise to  $104^{\circ}$  and even  $105^{\circ}\text{F}$ ., although the animals were, so far as could be determined, in good health.

below the normal just before death. When recovery ensues it falls as quickly to or even below the normal as it rose in the beginning of the attack. If the temperature be taken twice daily, in the morning and the evening, a new set of phenomena appear. The temperature at the outset rises during the day, is highest in the evening and may be low again in the morning. This oscillation, partly a normal occurrence, may be noticed for three or four days in some case, the morning temperature gradually rising until it is as high as the evening temperature. The high temperature then remains continuous until the end of the fever. These facts are well exemplified in the diagram on the following page. Fig. 1.

The fever may be detected by an experienced hand without a thermometer. The whole surface of the body feels hot to the touch. The heat is especially noticeable when the hand comes in contact with the anus or vulva in taking the rectal temperature. It is possible to go over a herd of cattle and select those having a high temperature by simply placing the hand on the anus.

The pulse and respiration rise with the fever. There is considerable variation in the number of the pulse beats and of the respirations during health, and there is also in some cases the excitement incident to being caught, which prevent our giving any very accurate figures. In health the number of respirations of the cattle used in our experiments may be put down as between 20 and 40 per minute, according to the temperature of the air and the age of the animal, while the pulse seems to range between 60 and 80 beats per minute.\* In animals in the acute stage of Texas fever the respiration may rise to between 60 and 100, and the pulse to between 90 and 110. As the fever subsides and recovery begins the great weakness of the animal still keeps the

\* The respiration in our cattle seems to have been higher than the normal of other observers. "Respiration in healthy cattle varies from 16 to 25 per minute, and may fall as low as 14 or rise as high as 30. According to the observations of Fürstenberg it is 21 per minute for cows and 24 for bulls."

The "pulse, like the respiration, varies greatly. According to Hering and Fürstenberg it is from 90 to 130 per minute during the first two weeks of life; from 70 to 80 from two weeks to two years. The average for a full-grown animal is 60, for old cows 50 to 55."—*Loc. cit.*



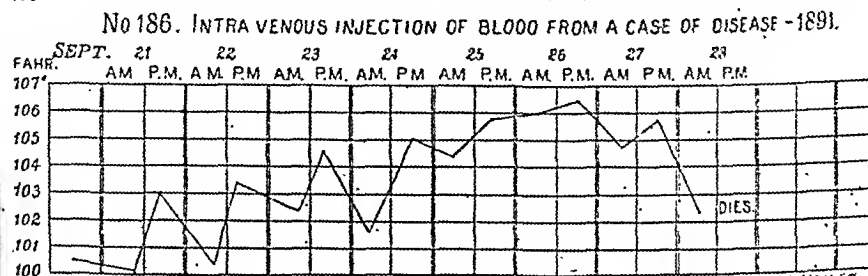
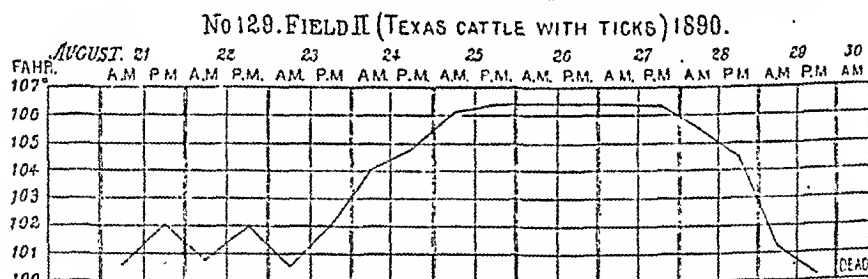
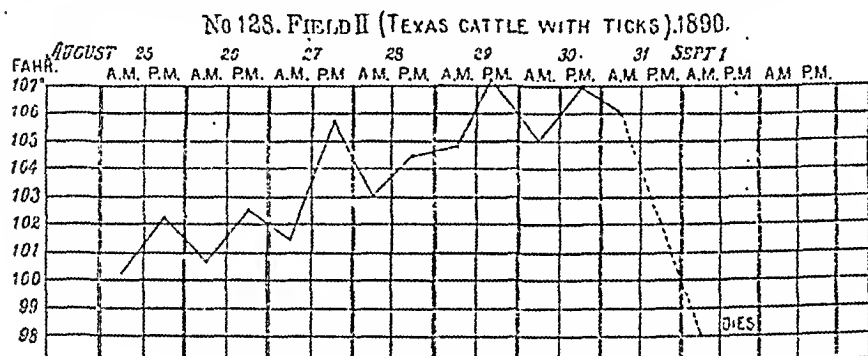
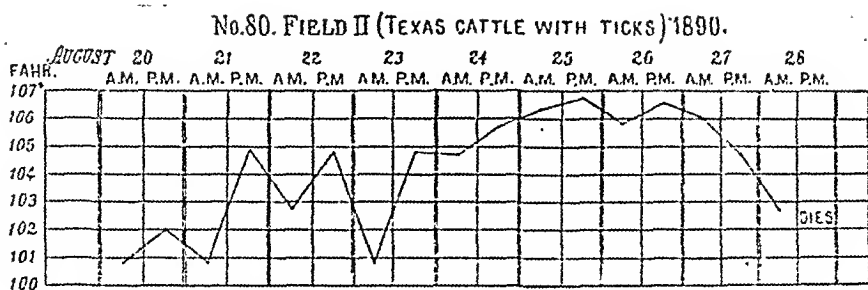


FIG. 1. TEMPERATURE CURVES IN FOUR CASES OF TEXAS FEVER

pulse very high for a time, especially when the animal is moved about or excited in any way. The respirations, on the other hand, are apt to fall below the normal in this same period. When death approaches the heart-beats increase in number as they grow feebler, and the respirations fall with the body temperature below the normal. These statements are fully illustrated in the appendix by the individual cases.

Next to the high temperature the condition of the urine demands our attention. The one sign regarded as peculiar and pathognomonic in this disease is the discharge of urine having the color of blood. This color is not due to a discharge of blood from the kidneys and subsequent breaking up of the red corpuscles, but to a filtration of the coloring matter of broken-down red corpuscles (hæmoglobin) already in solution in the circulation into the urine in the excretory structures of the kidneys. This fact was first pointed out in 1868 by R. Cresson Stiles. (p. 183) In using the term hæmoglobinuria this is all that is meant in this report. The precise state or condition of this coloring matter in the urine does not call for consideration.

Hæmoglobinuria may be said to be present in most acute fatal cases of Texas fever. Out of 46 fatal cases in which urine was in the bladder after death, hæmoglobin was present in 33 cases. In 13 negative cases the animals were killed in the earliest stages of the fever, or else they died or were killed after the number of blood corpuscles had been greatly reduced and the acute stage of the disease was over. In the former case the hæmoglobin had not yet been set free from the corpuscles; in the latter cases it had probably been eliminated one or more days before death. How frequently "red water" is passed before death we can not state with any degree of certainty, since its discharge may wholly escape observation. We have a record of hæmoglobinuria in but four cases: in No. 43 on the third day before death, in No. 44 on the fourth day before death, in No. 80 before it was killed (probably twelve to twenty-four hours before death), and in No. 198 twenty-four hours before death. In some of these cases it so happened that the urine was passed while the animal was undergoing examination. It is interesting

to note in connection with the statements made that in No. 44 no "red water" was found in the bladder after death, although it had been passed four days previously.

Whether hæmoglobinuria is always present in acute cases of Texas fever it is impossible to state definitely. As it seems to depend upon the rapidity with which the red blood corpuscles are infected and destroyed, a slower destruction may allow other organs to take charge of the debris and thus forestall the discharge of hæmoglobin in the urine. We have observed hæmoglobinuria in but one acute case which recovered, while in a number of cases in which the urine was collected, sometimes in the height of the fever, sometimes after it had departed, no hæmoglobinuria was detected. In this solitary case the high temperature first appeared August 18. On August 23 the temperature being still above  $105^{\circ}$ , the urine was free from hæmoglobin, but contained a small quantity (0.05 per cent) of albumen. On August 27 the temperature had become normal, but a second paroxysm followed soon after, and on September 4 and 5 the urine was of a port-wine color. Urine collected September 6 was again of normal color.

The urine during the fever, when free from hæmoglobin, contains in many instances a small quantity of albumen. The specific gravity may at first be high (1030-1040), and it may be strongly alkaline and effervesce with acids as in health, but, as the disease progresses and when the animal eats but little, its specific gravity will fall to 1010-1020; it fails to effervesce with acids and is faintly alkaline or even slightly acid. When the fever has subsided the urine has been observed to be in a few cases very watery, i.e., of very low specific gravity and feeble in color. Within one or two weeks, however, the normal condition is restored.

The urine which contains the coloring matter of the blood varies, as might be expected, very much in depth of color, according to the concentration of the hæmoglobin. It may have a very light claret color, or it may be so deeply tinted as to appear opaque and blackish. In a test tube when viewed by transmitted light it may barely permit the light to pass unless diluted with

water. (See Plate III, Fig. 4.) Such urine is, as a rule, entirely free from suspended matter and blood corpuscles. The latter may sometimes be found in small numbers when the urine is permitted to stand, and they may be derived from small (p. 184) hemorrhages in the pelvis of the kidney, quite regularly observed at autopsies. The coloring matter, as has been stated above, is derived from corpuscles broken up within the circulation, and not outside in the bladder. When such urine is treated with a little acetic acid a brownish flocculent precipitate, probably of the derivatives of hæmoglobin, appears. When boiled, a brownish flaky precipitate forms, which rises to the surface as a scum. As might be expected, such urine always reacts in presence of the usual tests for albumen. How much of the precipitate formed is the ordinary serum albumen found in various forms of kidney disease and how much belongs to hæmoglobin does not come up for consideration here. Suffice it to say that in very opaque urines the precipitate is quite abundant and corresponds when Esbach's test is applied, to from 1 to 3 per cent of albumen.\*

The subject of hæmoglobinuria is more fully discussed here under the symptoms because it is occasionally observed during life and probably with the aid of a catheter may be seen much more frequently. The causes of its occurrence and the way in which it is brought about will be discussed in connection with the microörganism. Very little need be said of the other characters of "red water." When found in the bladder after or collected shortly before death its specific gravity is usually low (1010-1020) and it is feebly alkaline or acid. There is no effervescence with acids. After standing, a few granular casts and rarely urates are found in the very slight sediment. The greater the number of days before death that it is collected the more nearly it approaches normal urine as regards specific gravity and alkalinity.

The bowels are as a rule constipated during the high fever, and on post-mortem examination the large bowels (cæcum and

\* If a few drops of acetic acid be added to urine holding much coloring matter in solution and allowed to stand over night, a clear yellowish liquid may be filtered off which gives the ordinary reactions for albumen.

colon) are found in some cases compactly filled with small, very firm, hard balls of dung. As the fever subsides the feces again become softer and are then found more or less deeply tinged with bile.

Loss of appetite always, and cessation of rumination usually, accompany the high fever after the third or the fifth day. These, together with the enormous destruction of the red blood corpuscles and the temporary disorganization of some of the vital organs, lead to a rapid loss of blood during the fever and even to extreme emaciation during the period following the fever. Some observers have recorded the sudden and partial cessation of milk secretion. We have had no opportunity to observe this symptom.

Symptoms referable to disturbances of the brain and the spinal cord were rarely noted. They usually manifested themselves in partial loss of vision, delirium, staggering gait, and swaying of the hind quarters. These latter may in part be referred to the great weakness which cattle manifest after some days of fever and perhaps to the œdema around the kidneys. This weakness may become so great that they will be unable to rise even when urged. When standing there may be noted a trembling of the muscles, especially of the hind quarters and limbs. Icterus or jaundice has not been noted in any case during life.

Another character of this disease, the most constant and valuable of all, and of which the hæmoglobinuria or "red water" is but a part, is the thinness of the blood. A more thorough discussion of its condition will be given further on. In this connection we only mention those phenomena which can be witnessed by the naked eye. Soon (p. 185) after the high temperature sets in, the blood begins to grow thin, and after some days of fever it has become very pale and watery. An incision into the skin readily shows this to be the case. The difference between the drop of rich red blood issuing from a slight cut of the skin in healthy cattle, and the thin, pale drop oozing from such a cut in Texas fever, is very marked. This difference is due to the loss of red corpuscles, which give the blood its characteristic color. Associated with this there may be in some cases a marked blood-

lessness of the skin in the latter stages. A number of small incisions are often required to obtain a few drops of blood. In some cases shortly before death the blood slowly trickles from a slight incision for some time before it is checked by the natural process of coagulation.

When freshly drawn blood is allowed to stand the serum forced out of the clot has in the acute stage a very dark red color, indicating the presence of much coloring matter in solution. As regards the coagulability, which some observers have regarded as feeble, we have no facts pointing in one direction. In a few cases the coagulation appeared retarded; in others it appeared to be normal in rapidity and effectiveness. As will be seen further on, the condition of the blood must vary considerably from time to time. At one time it may contain the *débris* of destroyed corpuscles equal in number to one-tenth, or even one-fifth, of all circulating in the body. That under such circumstances its coagulability may be affected is evident. Frequently, however, the blood comes under observation when the destruction of red corpuscles has ceased and the products have either been excreted or metamorphosed. In this way conflicting observations may perhaps be harmonized. In general, we may say that the coagulability of the blood is not much altered.

We have thus briefly sketched the symptoms of an acute attack of Texas fever and noted three important diagnostic features, high temperature (or fever), hæmoglobinuria (or red water), and thinness of the blood (or destruction of red corpuscles). The last is the most constant, and, in fact, the one essential character of Texas fever. Among the other less important symptoms and appearances, many of which are always associated with one or the other of those mentioned, are dry, hot skin, high rate of pulse and respiration, loss of appetite, cessation of rumination and of milk secretion, constipation, hyperaemia followed by bloodlessness of the skin and mucous membranes.

The course and the duration of the disease are subject to variations. We have seen that it begins somewhat abruptly with a high temperature, runs its course in a few days, and terminates fatally, or else it disappears as quickly. In the latter case the

disease is followed by a period of great debility, owing to the impoverished condition of the blood and the degenerative processes set up in the various vital organs, and not infrequently by relapses. Some animals never fully recover; in others recovery takes place after weeks and months.

The duration of the disease varies more or less, but the continuous high temperature rarely lasts longer than eight to ten days. The fatal termination may take place in the height of the fever—that is to say, four or five days after the appearance of a high morning temperature, and may be the direct result of the derangement of the vital functions, due to the rapid destruction of red corpuscles by the microorganism, or it may take place after the fever has subsided, when the animal fails to rally from the shock imparted to the system and from the drain of its blood-forming resources. If we take as our starting point of the fever the first high morning temperature death may ensue from four to (p. 186) fourteen days thereafter, or it may be delayed still longer, when the animal dies slowly of exhaustion. The period of disease for such as recover is practically the same. A fever period of eight to ten days is followed by a period of normal or subnormal temperature. The falling of the temperature marks the end of the destruction of red blood corpuscles and the disappearance of the parasite from the blood. The subject of relapses and secondary attacks during the season by which the period of disease as a whole may be prolonged into months is discussed further on.

The mortality from Southern cattle fever varies greatly, as will be seen in the following pages on the mild chronic form of the disease. The time of the outbreak will largely decide whether practically all the attacked animals die or all survive. A mid-summer outbreak, when acute in its nature, is the most fatal. From this there may be all gradations towards the mild, non-fatal form of late autumn.

#### MILD, NONFATAL, OR CHRONIC TYPE

This type of Southern cattle fever has hitherto remained unobserved. The reason for this is quite simple. It can be recognized only by an examination of the blood, which must determine

the presence of the microparasite in the red corpuscles and their approximate rate of destruction.

The mild form of Texas fever is largely a disease of autumn, after the heat of summer has passed away. In the latitude of Washington, D. C., October and November, rarely the first week of December, are favorable to it. It is not, however, strictly limited to this period, as it may be observed from early August on through the entire season. Its occurrence during this latter period, which is commonly characterized by acute disease, is limited largely to the less susceptible calves and to a very few of the exposed adults. Cattle which have passed through the acute disease may have a relapse in the form of the mild type in autumn.

The essential difference between this and the acute type rests on the fact that a stage of the parasite circulates in the blood of the mild cases, which is different from the one observed in acute cases. This difference will be made clear in the chapter on the Texas fever parasite. When we come to the various symptoms there is only a difference of degree. The fever temperature is low and fluctuating, rarely rising above  $105^{\circ}\text{F}$ . in the evening. In the morning the temperature is usually normal or very slightly elevated. The destruction of red blood corpuscles by the microparasite goes on as in the acute form, but much more slowly and deliberately, and hence the period of disease itself—that is, the time during which the parasite is present in the blood in considerable numbers—is much prolonged. The hæmoglobinuria is probably never present. The various symptoms which accompany the fever are only present when the temperature is above  $103^{\circ}\text{F}$ . There is loss of appetite and dullness, especially when the number of red corpuscles has reached its lowest limit, followed by a slight falling away in the condition of the animal.

It will thus be seen that there are no symptoms manifest to the unaided eye which we might put down as characteristic of Texas fever in its mild type. It might be confused with a variety of disorders incident to the bovine species or else be entirely overlooked. From an economic point of view it is of not very great consequence, since it is not fatal, and the loss in weight, though



quite considerable in some cases, is soon made up in the winter months.

(p. 187)

THE RELATION BETWEEN THE ACUTE AND THE MILD TYPE OF TEXAS  
FEVER—RELAPSES

In certain cases it was noticed that after the animal had recovered from the acute attack, and the number of blood corpuscles had nearly reached the normal maintained before the attack, it would again fall, and in the blood many corpuscles could be found containing the small stage of the Texas fever parasite which is always associated with the mild type. In other words, the acute attack would be followed after a certain interval of time by a mild attack. This interval may vary considerably. Thus, in one case the acute attack began early in August and the secondary, or mild attack, about one month later. In another the acute attack began early in September, the mild attack about three weeks later. In a third, the acute attack began near the middle of August; the mild attack was observed in the second week of October. Two cases of Texas fever, induced by the intravenous injection of blood, are particularly noteworthy in this respect. In one the disease began July 13, in the other, July 23. In both the mild attack was detected at the same time at the end of August, although it may have begun some days before.

The question naturally presents itself whether these secondary attacks are simply relapses or whether they are reinfections from without. As will be fully discussed further on, the young cattle tick induces the disease in natives as soon as it has attached itself to their skin. Since the cattle ticks are present on the infected field during the entire summer and autumn it is reasonable to suppose that the secondary or mild attacks may be caused by ticks which have remained on the field or by the second generation, since the usual time for mild attacks, late September and October, is the time for the appearance of a second generation of young ticks. Whether these mild attacks are always due to an invasion of the animal by such a second generation, or whether

they may be due in some cases to the recrudescence of the micro-organism not yet entirely eliminated from the system, was settled by the two cases above referred to. Since they were inoculated but once, and there was no opportunity for reinfection, these cases prove that a mild attack may follow an acute attack without a fresh importation of the microörganism from without; in other words, that the mild attack may be considered as a relapse. The conclusion does not operate against the probability that some mild attacks may be due to secondary infection from without.

In addition to the true relapses just referred to, we may observe more or less oscillation in the course of the disease as expressed by the destruction of red corpuscles. This oscillation is probably dependent on the periodical multiplication of the micro-parasite, and in this respect may be regarded essentially identical with the relapse. The latter follows the primary disease at long intervals, while the oscillations are but one and one-half to two weeks apart as a rule. Neither the relapses nor the oscillations have been marked by any distinctive clinical signs excepting a slight rise of temperature in some instances. Such undoubtedly do exist, and may perhaps be detected by more frequent daily measurements of the temperature and a closer and more frequent examination of the animals and their excretions than our time has permitted us to make.

#### PATHOLOGICAL CHANGES

In dwelling upon the pathological changes caused by Texas fever we have had two objects in view: first, to add as much as possible to the information already on hand, and, secondly, to furnish such a complete (p. 188) record of the cases in the various experiments that there would be no room for doubt in the reader's mind that we were dealing with Texas fever wherever this is claimed to be so. Inasmuch as the causation or etiology was the essential object of the researches, everything else had to be subordinated to lines of investigations which endeavored to get at the cause and the modes of transmission of the malady before us. The following account, though somewhat meager for this

reason, is given as a description of the nature of the disease we were dealing with. We may note here that the lesions induced by North Carolina cattle and those induced by Texas cattle at the same season were identical in every respect.

#### CHANGES IN THE ORGANS AND TISSUES

Cattle which have succumbed to Texas fever undergo post-mortem changes very rapidly. This may be largely due to the fact that the disease occurs in the greatest heat of summer. Hence facts relating to the appearance of organs and tissues are of doubtful value if the animal has not been examined soon after death. This occurs as a rule during the night, and post-mortem changes were begun when the morning arrives. It is frequently desirable, therefore, to kill animals in different stages of the disease to obtain trustworthy facts.

*The skin* presents nothing abnormal to the unaided eye, and, as will be pointed out later on, certain regions are beset with ticks. In one case which came to our notice very recently the hair on the abdomen and the inner aspect of the thighs was matted into little tufts by dried blood. The skin showed at such places a bluish elevated spot, and when incised a little blood was found in the subcutis. This may be what has been called blood sweating.

The subcutaneous tissue and fat in our cases were free from any changes except in three, in which they were of a decidedly yellowish tinge. Jaundice was thus of rare occurrence. In the report of the Metropolitan Board it is stated that "the fat has a deep or high colored greenish appearance and has not the firm resistance of health. The lean meat is of a brownish mahogany color, and on being cut into has a peculiar sickening odor." The muscular tissue in our cases was normal in color or perhaps a trifle paler. (Edema of the subcutaneous tissue of the ventral aspect of the body was occasionally present and referable to the debilitated condition of the animal.)

*The brain* was removed in a small number of cases and carefully examined, but no lesions which can be regarded in any

sense as peculiar to or characteristic of the disease were observed. It may be said, in general, that the brain shared the general tendency towards the injection of the capillary system. The vessels of the pia and the plexuses were engorged, and over the frontal lobes and near the great transverse fissure it was more or less pigmented—a condition also met with in other diseases. The gray matter of the cerebrum and especially of the cerebellum appeared of a more pinkish color. The white substance was normal in color, the ventricles free from fluid.

*Lungs.*—The lungs are, as a rule, healthy. There is, in many cases, pulmonary edema, with or without emphysema, noticeable after death. In a few instances foci of dark red hepatization were observed in one of the principal lobes, which involved one or several lobules.

*Heart.*—At the autopsy the right ventricle is always distended with blood, fluid or clotted, according to the time elapsing between death and the examination. The left ventricle is usually firmly contracted, and may contain a small quantity of fluid or clotted blood. The clots are quite firm and very rarely mixed with firmer, pale yellowish clots. (p. 189) A very constant lesion is the extravasation of blood beneath the epicardium and endocardium. This is mainly restricted to the left ventricle, although petechiae are not infrequently met with on the right ventricle. On the external surface of the heart the petechiae are usually grouped along the interventricular groove and near the base, although cases occur in which the whole ventricular surface is sprinkled over with them. The inner surface of the left ventricle shows larger patches of extravasation usually on, or at the base of, the papillary muscles. On the large vessels at the base of the heart, within the pericardial sac, there are frequently very delicate shreds of tissue or patches in a hyperaemic condition. The heart muscle, on closer inspection, is observed to have its minute vessels markedly injected, and in fresh sections the capillary network is found densely packed with red corpuscles. In cases which have succumbed after the subsidence of the fever the heart muscle is quite pale. Cloudy and fatty

changes of the fibers are in some cases quite marked; in others absent or restricted to a small number of fibers.\*

Lesions of the abdominal cavity are not infrequent. Edematous conditions are quite common around the kidneys and will be referred to again. Gelatinous edemas are sometimes encountered in the portal region between the duodenum and liver. The omentum frequently displays peculiar hyperaemic patches, consisting of delicate shreds of vascular tissue made visible to the naked eye by the injected condition of the blood vessels.

*Spleen.*—That this organ in Texas fever is very much enlarged was commented upon by the earlier observers, and the name "splenic fever" took its origin from this condition. Gamgee, in 1868, caused to be weighed the spleens of a large number of native Western cattle, of Cherokee cattle (supposed to have come from the Indian Territory), and of Texan cattle. These animals were considered healthy and fit for human consumption.

The average weight of the native Western spleen was 1.45 pounds; of the Cherokee spleen, 1.94 pounds; of the Texas spleen, 2.5 pounds.

A number of spleens were weighed at one of the Washington abattoirs to determine the normal weight. The result is given in the following table:

Date	Weight of steer	Weight of spleen
	<i>pounds</i>	<i>pounds</i>
October 10, 1890, No. 1.....	950	1.75
October 10, 1890, No. 2.....	900	1.75
October 10, 1890, No. 3.....	1,000	1.90
October 10, 1890, No. 4.....	1,000	2.37
October 10, 1890, No. 5.....	1,000	1.50
October 15, 1890, No. 6.....	1,300	2.25
October 15, 1890, No. 7.....	1,100	1.75
October 22, 1890, No. 8.....	1,400	2.00
October 22, 1890, No. 9.....	1,300	1.90

\* An interesting appearance, which may now and then deceive observers, is the presence, under the endocardium, of minute whitish, fusiform bodies, perhaps one millimeter long, which seem to follow the course of the superficial veins and rest upon or near their walls. They are sarcosporidia (psorospermia) cysts filled with falciform bodies. These

The source of these animals was not determinable. It will be noted that the weight varies considerably, although in all the appearance of (p. 190) the organ, both as to its capsule and pulp, was the same. The weight of each animal was estimated by the butcher in charge. These examinations were made at a time when any destructive influences of the summer on the blood may not have been entirely neutralized. How far the bleeding of the animals at the time of slaughter may have affected the weight of the spleen in comparison with that of cattle which succumbed to the fever with the blood in their system it is of course impossible to estimate. By taking the average of the above nine cases, the weight of the spleen of a steer weighing 1,000 pounds would be 1.72 pounds.

The weight of the spleen in Texas fever varies considerably, according to the stage of the disease in which the animal succumbs. Animals which die after some days of high fever have usually the largest spleens, although this is not an invariable rule. If we compare the weights of spleens as given in the appendix under many of the cases it will be seen that in acute cases the spleen is generally from two to four times its weight in health.

If we turn for a moment to examine its appearance we find its general shape unaltered, but the ordinarily rather thick whitish capsule very much distended and attenuated, so that the dark pulp shows through it very distinctly. (Plate I.) The veins of the capsule are distinct, the minute vessels markedly injected and occasionally accompanied by extravasations of blood. The organ is firm to the touch, owing to its distended condition. When it is incised, the pulp appears as a dark brownish-red, glistening, homogeneous mass, which has been compared to "blackberry jam" in its appearance. The usual markings of the parenchyma of the normal spleen are effaced. The grayish Malpighian bodies and the whitish trabeculae have all disappeared from view within the distended pulp. (The differences between the cut surface of the spleen in health and in Texas

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cysts are likewise present in the depths of the heart muscle and in the skeletal muscles. Under the endocardium their number is greatest in old cows. They are in some cases so numerous that fifty may be included in an area of a square centimeter. They are easily removed entire by careful teasing.

fever are well brought out on Plate I.) The pulp may be still firm, or it may be partly diffuent, welling out as a semifluid mass from the incised retracting capsule. It has occasionally been reported as ruptured, but this may be a combination of post-mortem softening with carelessness in its extraction. In some cases the spleen may be much heavier than in health, but its markings still visible on section.

A microscopic examination shows that the enlargement and peculiar color of the spleen tissue is due to an engorgement with red blood corpuscles. With this engorgement there may be associated a variable number of large cells containing coarse granules and from two to twelve red corpuscles, or else the remains of these corpuscles in the form of irregular clumps of yellowish pigment. The pigment is also free in masses of variable size. Examination of fresh pulp from spleens of healthy cattle showed that the presence of large quantities of free pigment of the form described is not uncommon.

Of all the organs *the liver* is the most seriously involved. (See Plates II and III.) The enlargement, congestion, bile-injection, and fatty degeneration were pointed out by R. C. Stiles in 1868. Gamgee limited himself to matters of weight, and evidently did not observe the extensive changes which the parenchyma underwent. In our own observations of healthy and diseased livers, the latter were probably from 3 to 5 pounds heavier than the former. The edges were well rounded off. The color of the surface was usually paler than in normal livers, and in most cases of a peculiar mottled appearance. The mottling was due to minute irregular grayish-yellow patches usually 1 millimeter or less in diameter. When incised the parenchyma was remarkably bloodless in most cases, and a lac-colored, thick blood poured (p. 191) from the cut ends of the larger hepatic veins. The color of the cut surface was either a uniformly brownish yellow or else mottled as on the surface. (Plate II, Fig. 1.) The mottling, on closer scrutiny with the naked eye or hand lens, was found to be due to a paler yellowish discoloration of the zone bordering the intralobular veins. (Plate II, Fig. 2.) This zone of discoloration was the wider the more prolonged the disease, and in a few cases

involved the entire lobule. Parallel to this degenerative process the consistency of the organ became less resistant, more doughy, and brittle.

In thin sections of fresh tissue\* the most striking phenomenon was the filling up of the ultimate bile canaliculi, so that the hepatic cells were inclosed in polygons of yellow lines forming a beautiful network. (Plate III, Figs. 1 and 2.) When the liver is teased and crushed the contents of these bile canaliculi may be found floating free in the form of rods, sometimes with Y-shaped ends. (Plate III, Fig. 3.) This stasis or filling up of the ultimate bile capillaries was present in nearly all animals examined. It was most pronounced in those whose death followed quickly after a high fever. In one case purposely killed in the early days of the fever the liver was the seat of marked congestion, the bile-stasis not having taken place yet. The extent of this stasis varies considerably. It may be seen in small isolated areas or else it may involve a large continuous territory. Owing to absence of connective tissue between the lobules it is quite impossible in fresh sections to make out accurately its distribution. It seems to be most frequently met with in the innermost or hepatic zone of the lobule (Plate III, Fig. 1; Plate II, Fig. 4.), but it may also be found involving the entire lobule. Small bile ducts between the lobules are often found injected, and rarely lines of yellow injection may be visible to the unaided eye.

Associated with the occlusion of the biliary canaliculi and ducts is a more or less extensive fatty degeneration of the hepatic cells. This is most advanced in prolonged cases of disease. In several which came under our observation the fatty changes were so extensive that cells free from large quantities of fat could not be seen. Among other abnormal appearances may be mentioned the presence of irregular yellow clumps of pigment in the hepatic cells, and of stellate masses or blood-red needle-like crystals (Plate III, Fig. 2) of very minute size (haemoglobin?). In one case large-branched thrombi were found in some of the hepatic veins.

\* These were usually made with a razor, and examined in iodized serum. The freezing microtome was not generally used, because it was desirable in this examination to preserve the red corpuscles.



The pathological changes observed in sections and teased preparations of fresh liver tissue are more accurately interpreted in sections of tissue hardened in Müller's fluid and in alcohol. The material was imbedded in paraffin after having been passed through chloroform paraffin. Sections cut in this way were far more serviceable than those cut in alcohol. The injection of the bile canaliculi is seen only in Müller's fluid preparations or in alcoholic material cut directly without imbedding. The extent and location of the injection are variable. It may appear over an entire lobule or only a small portion of it. The fatty degeneration so regularly seen in fresh material shows itself in sections of hardened material in a peculiar vacuolated appearance of the cell protoplasm, the fat having been dissolved out. The vacuolation may be more pronounced near the center of the lobule, where the individual vacuoles may be as large as red corpuscles. Of these there may be several in a single cell, very little of the protoplasm remaining. The (p. 192) cell protoplasm of the peripheral zone of the lobule is uniformly vacuolated, the vacuoles being very small.

Another change that is of considerable importance in estimating the pathological effect of the disease is a tendency toward necrosis of the inner zone of the lobule. This process, which shows itself to the naked eye as a faint paler mottling of the liver tissue limited to the inner zone of the acini, seems to begin around the central vein and extend toward the periphery.\* It is characterized by a degeneration and loss of the nuclei of the parenchyma cells. These changes are observable with various stains, such as haematoxylin, alum carmine, and the anilines (alkaline methylene blue, aniline water-methyl violet, etc.). Ehrlich's acid haematoxylin, with or without eosin, is a very satisfactory dye, owing to the intensity of the nuclear staining. The changes undergone by the nuclei are at first manifested by a feebler stain. The margin, which may be irregular, is stained, but the body of the nucleus is

\* One may be at a loss to determine the limits of the lobules in the ox, owing to the absence of any complete connective tissue boundary. In stained sections they are readily made out by taking as a guide the connective tissue with its numerous stained nuclei in the spaces in which the interlobular vessels and ducts pass.

pale, and usually contains several deeply stained round bodies stimulating nucleoli. Later on these bodies are all that is left. They shrink together or even unite into a small irregular deeply stained mass. The cell protoplasm is much more feebly stained than in normal areas and its outlines are indistinct. This nuclear degeneration may appear in a compact area uniformly, or we may find all grades of degeneration intermingled.\* In tissue undergoing such changes the central portions of each lobule may appear much paler than the peripheral. The trabecular arrangement of the cells may be exaggerated by a widening of the lumen of the capillaries in the periphery and made indistinct or become obliterated in the central portions. The destructive changes in central regions may go on to a complete loss of the nuclei. This appears very well in methylene-blue stains. The necrotic portion refuses to stain at all, and the result is a mottled section with the isolated unstained areas inclosed in an irregular network of stained material very striking even to the naked eye. Such mottling will, of course, appear with other stains, but not so distinctly. The extent of the necrosis may be as much as one-third or one-half of the entire volume of the lobule.

In endeavoring to account for the fatty and necrotic changes of the parenchyma we think it probable that the bile stasis, by plugging up with solid bile the ultimate bile canals, may interfere in some way with the nutrition of the parenchyma, or exercise upon it some deleterious influence through the stagnating bile, and thus set the degenerative processes in motion. The bile stasis is undoubtedly due to the breaking up in the capillaries of the liver of immense numbers of infected corpuscles. A large amount of debris is thus brought to the cells for transformation into bile. The result is an abnormal fluid containing a superabundance of solids (pigment) which is unable to flow in the bile channels. How far the degenerative process may be aided by any plugging of the capillaries with infected corpuscles it is impossible to state. In fact, the relation of the disintegra-

\* J. H. Detmers (5, p. 137) observed in 1883, the disappearance of the nuclei and the reticulated appearance of the cell protoplasm. Babes, in 1889, described a similar condition in Roumanian cattle affected with infectious haemoglobinuria.

tion of the red corpuscles and of the bile stasis to the fatty degeneration and the necrosis around the central vein should be made the object of special pathological study.

(p. 193) *Bile* is found in the gall bladder in considerable quantity (one-half pint to a quart) after death. As might be anticipated from the description of the changes in the liver, this fluid is greatly altered. The usual limpid greenish fluid is replaced by an almost semisolid mass. As it flows from the incised bladder it has been aptly compared to chewed grass. The presence of mucus makes it cohesive enough to be drawn out into long flat bands as it flows. When it is allowed to stand quietly in a cylindrical vessel a layer of flakes settles down which occupies not infrequently one-half of the entire column. The supernatant fluid is much darker than normal bile. The suspended matter appears to be made up chiefly of small yellowish flocculi or flakes. A deep yellow tinge is imparted to all vessels and to the hands coming in contact with it. When examined under the microscope the suspended particles are resolved into amorphous yellowish masses mingled with bright golden points barely visible at 500 diameters. The common bile duct has always been found pervious, and in many cases an abundance of bile is found in the small intestine.

*The kidneys.*—We have in a preceding chapter referred to the condition of the urine in this disease, and have found it altered by the presence of certain abnormal products—hæmoglobin and albumin. We might therefore anticipate more or less alteration in the secreting organs, the kidneys. In a considerable number of cases a sero-sanguinolent condition of the connective tissue and fat about the kidneys is observed. In a few cases the ventral surface of the organs appeared like two large blood blotches. The portion of the abdominal wall upon which the dorsal surface of the kidneys rests is free from these effusions.

The kidneys themselves, like the other organs affected by this disease, vary more or less in color, according to the severity and stage of the disease. In those cases which succumb early in the fever, and in which the bladder is filled with port-wine-colored urine, the kidneys are enlarged and of a uniform dark brownish-

red color throughout. The usual markings are pretty well effaced. When fresh sections are examined from different regions, the vascular system is found quite uniformly engorged and distended with red corpuscles. The section is likewise sprinkled over with very minute pigment particles. Sometimes irregular masses of red corpuscles, run together as it were, are met with in the vessels of the pyramids. Lesions of the secreting structures are not discoverable. Hemorrhages are uncommon. In those cases which succumb after the hæmoglobinuria and the fever have passed away, the kidneys are paler than usual and the texture is quite flabby. Sections of the fresh tissue show in the cortex a considerable amount of pigment. In some cases the convoluted tubules are the elected seat of pigment deposit, and the epithelium of these tubes may be so filled with yellowish red pigment that they are easily traceable in their windings by their decided color. Fatty changes are occasionally met with in the epithelium, and the straight tubules of the pyramids may be filled with fat globules. Degenerative or necrotic changes of the epithelium were not noticed in sections of hardened tissue from a few cases stained in various ways. In those cases in which the capillaries were filled with red corpuscles, the latter were usually all infected with Texas fever parasites.

The pelvis and its ramifications were usually found beset with blood extravasations. It has already been remarked under the head of symptoms that in most cases the bladder is found containing from one to four quarts of urine holding more or less hæmoglobin in solution. Under the same head will be found a full discussion of this phenomenon, (p. 194) so that it need not be touched upon here. The bladder itself may show a few ecchymoses on its inner surface.

*Digestive organs.*—The upper portion of the digestive tract, including the paunch and reticulum, is generally free from morbid changes. The third stomach or manyplies was, in a few cases, somewhat "impacted"; that is, the contents were firm and rather dry, and the superficial layer of epithelium of the lining membrane tended to peel off. In most cases it was normal. The fourth or true stomach (abomasum) shows not infrequently a

hyperaemic condition. In some cases the laminated portion was of a uniformly bluish-pink color. Both Gamgee and the Metropolitan Board of Health of New York City have laid much stress upon the lesions observed in this organ. Gamgee describes in addition to the general hyperaemia three kinds of lesions of the laminated, cardiac portion. He finds in some cases petechiae, "resembling flea-bites" in some respects, whose "center is dark and sometimes softened and perforated." In others "the reddened folds are studded with minute yellowish-gray granulations due to a change in the epithelium, which becomes swollen and has a tendency to drop off. Each granulation does not usually exceed the size of a pin's head. This appearance is most marked where the folds are most congested, and in some cases where the congestion is slight it requires a somewhat careful inspection to recognize the presence of this change." The third lesion is described as follows: "Scattered throughout the folds, especially near their free edged, we find . . . marked erosions, as if the epithelium had been peeled off with a sharp finger nail."

The lesions described as the second was also present in many of the cases recorded in the appendix. Its constant appearance was very puzzling and might readily lead one to suspect some relation to the disease. Many of the granulations had their center perforated so that they suggested the presence of enlarged glands with hyperplasia of the tissue surrounding the mouth. It was not until the fall of 1890 that the nature of these little elevations was solved. In an animal killed for some purpose, though free from the disease, marked lesions of the mucous membrane of the fourth stomach were found. These consisted of yellowish-white exudations about as large as split peas, viscid and composed of round cells mixed with mucus and associated with the mouth of these elevated spots. A careful microscopic examination of this exudate showed the presence of a very minute nematode, a strongyle, imbedded in the exudate. That this was the cause of these lesions was soon determined. Some sections of the fourth stomach of a case of Texas fever in which these lesions were present had been prepared some time ago, but had not been studied, for want of time. These were now ex-

amed, and in the minute pits corresponding to the perforation in the center of these granulations the worm was seen coiled up at the base of the epithelial layer. It was also recognized as the worm found and described a few months before by Ostertag in cattle slaughtered in Berlin, Prussia. The worm described by him was larger, but the fact that it produced the same lesions made it highly probable that the two strongyli are of the same species.\* This disposes of the second lesion seen by Gamgee. As regards the first, it is not unlikely that it represents the earliest stage of the invasion of the mucous membrane by the worm, but we will not be dogmatic on this point.

As regards the erosions, it may be said that in a small proportion of (p. 195) our animals, irregular, very shallow, flattish excavations of the mucous membrane were found which has a blackish base. They varied much in size, some being quite small. They were most numerous on the laminae. Some were occasionally encountered in the pyloric portion. After finding these same erosions even quite abundantly in some healthy stomachs from an abattori we interpreted them simply as traumatic erosions due to the accidental presence of some foreign body.

In the investigations of the Metropolitan Board in 1868, the pyloric portion of the fourth stomach was found in many cases to contain deep, ragged excavations with hemorrhagic base. It is not improbable that at least some of these may have been the result of vascular occlusion, since in the animals examined at that time there seems to have been, so far as the descriptions and illustrations go, much more congestion of the fourth stomach and intestines than in our own cases. These erosions were extensive in but one case of ours. Their constancy led Moreau Morris in his report to the Board to consider them as a more certain indication of Texas fever than the other lesions commonly present. With this we can not agree. In fact we regard the digestive lesions as perhaps the least pathognomonic of the disease.

\* Ostertag named the worm *Strongylus convolutus*, but this was changed by Dr. C. W. Stiles, of this Division, who gave some attention to the worm subsequently, to *Syringylus Ostertagi*, Journ. Comp. Med., 1892, p. 147.

In a few cases affected with a more or less chronic after disease, there was much oedema of the coats of the fourth stomach, extending also to the mesentery.

The lesions of the intestines are limited to hyperaemia and pigmentation. Beginning with the duodenum, there is found generally an abundance of bile and more or less injection and pigmentation of the villi appearing in the form of closely set points and fine lines. The remainder of the small intestine may show with the stomach more or less marked congestion, or there may be patches marked by the injection of minute vessels. In many of the cases examined the mucosa was pale and concealed by a thin layer of a grayish pasty consistency made up largely of desquamated epithelium. The walls of the lower half of the small intestine contained quite invariably small worm tubercles. These appeared from the serous surface as dark blueish, slightly elevated nodules. In passing the opened intestine between the fingers the mucosa was found intact, while the tubercles gave one the sensation of small shot in the walls. They harbor a parasitic worm and have nothing to do with the disease.

In the large intestine we find more or less hyperaemia and pigmentation in longitudinal lines corresponding to the summits of the folds of the mucous membrane. This condition is more marked in the caecum and rectum than in the colon, and seems to be associated with the constipated condition. Thus, the cecum is in some cases distended with very hard, dry, fecal balls, and some may be found in the rectum. In some cases no abnormal condition of the large bowel is discoverable.

*Differences in the pathological changes of our cases and those studied by former observers.*—We have already called attention to the fact that, while jaundice was rare in our cases, it has been rather common according to other investigators. In fact it has been named "the yellow fever of cattle" on the strength of this symptom. Attention has also been called to the lesions of the fourth stomach in this respect. The causes for these differences may perhaps be looked for in the different condition of the animals examined. The Metropolitan Board in 1868 examined cattle which had been traveling and had undergone much hard

ship both by rail and on foot. They were all western animals, which succumbed soon after their arrival in New York. How far the deprivation of food and water, the crowding, the constant motion, and (p. 196) the marching may have contributed to a more active circulation and to an absorption of the obstructed bile from the liver into the blood must remain a conjecture. In our cases the animals were simply pastured and the frequent blood examinations as well as the taking of the temperature were carried out with the least possible disturbance to the animals. Again the animals used by us weighed between 500 and 800 pounds. They were not more than average animals in an average condition of flesh. It may be that the large fat animals in a plethoric condition would develop the peculiar condition of the muscular system, the jaundice and the more marked hyperæmia (and sloughing?) of the fourth stomach and intestines observed in 1868. The essential lesions, however, are precisely the same. The disease first studied by Gamgee and the Metropolitan Board of Health in 1868 is the same as that now occupying our attention. The changes going on in the blood, the liver, spleen, and kidneys are so striking and peculiar that they could not very well belong to two different maladies.

#### CHANGES IN THE CORPUSCULAR ELEMENTS OF THE BLOOD

The condition of the blood, so far as determinable by the naked eye, has already been referred to. It grows very thin and watery as the disease progresses. This fact was emphasized by the earliest students of this disease, the investigators of the Metropolitan Board in 1868. Its prime significance seems to have escaped them and subsequent ones. In the preliminary pathological examination of four cases in 1888 the destruction of red corpuscles explained, best of all, the conditions observed. Hence the importance of concentrating the attention on the blood and its cellular elements was at once recognized. In 1889 arrangements were made by which cases of the disease could be studied during life at the experiment station, and within easy reach of the laboratory, in the District of Columbia. In order to measure in some accurate manner the changes going on in



the blood, the red corpuscles were counted as soon as living cases were accessible. The result proved surprising in the extreme. It was found that there is a destruction of red corpuscles going on from day to day quite enormous in acute cases. Going parallel with this diminution in the number of corpuscles a change in their size and appearance became manifest which demanded a careful study in order that a distinction between the stages of the intraglobular parasite and the altered corpuscles which might be confounded with them could be made. As the investigations proceeded an accurate knowledge of these changes proved very valuable as a means of diagnosis. In a number of cases the recent existence of Texas fever could be at once determined by their presence, even though the Texas fever parasite was no longer to be detected in the blood. These changes must now be considered as next in importance to the parasite itself in the diagnosis of Texas fever in all its forms. The present chapter is therefore a consideration of the changes, both quantitative and qualitative, affecting the red corpuscles without reference to the micro-parasite accompanying them. This will be described in another chapter.

#### THE DESTRUCTION OF RED BLOOD CORPUSCLES

The red corpuscles were counted with the apparatus of Thoma, constructed by Zeiss. In the direction for use accompanying the apparatus it is suggested that 200 spaces should be counted in order to reduce the errors to a minimum. Owing to the large quantity of work that had to be done in connection with the various field experiments to be (p. 197) described, the counting could not be carried to the point of accuracy indicated. Moreover, the quantitative changes in this disease are so gross that a slight error will not affect the comparative results. The method adopted was to count 40 spaces. Two parallel rows of squares through the ruled field were counted. Such rows were chosen through which an additional line was drawn in order to guide easily the eyes. Hence these rows were always four squares apart. By counting the red corpuscles in a row of squares any differences in their distribution from one side of the cell to the

other were thus averaged. A comparison of the results of counts in the case of healthy controls, or of animals before the onset of the disease, shows a remarkable uniformity of results. Moreover, successive counts either from the same dilution or from separate dilutions of blood from the same animal collected at the same time, showed that the greatest margin of error was one to two hundred thousand, a comparatively insignificant figure in the work before us.

It was necessary also to make a modification in the collection of blood. The uneasiness of many animals, the presence of flies, the heat and wind on the fields made it necessary to act with great rapidity. Hence the complete filling of the capillary tube was dispensed with. Only a fraction of the length was filled with blood, usually from 0.6 to 0.9. The quantity aspirated was at once noted and the 3 per cent salt solution of Toison's fluid was drawn up to the mark indicated. In those cases in which the blood was very thin and the various squares contained only from 0 to 3 corpuscles about 80 squares were counted.

If, in the collection of the blood, the dilution with the salt solution of Toison's fluid, its proper mixing with the blood, and especially the placing of the drop in the cell, be properly carried out, the necessity for counting a large number of squares is made nugatory. Special care should be devoted to the cleaning of the glass cell and cover and the keeping away of all dust. When the coverslip has once been laid on the cell it should not be slid or moved about, so that the uniformity of distribution is not disturbed. The process of collecting the blood for counting is as follows:

In most cases the animals could not be removed from the field, and the examination of the blood had to be proceeded with on the field itself. The various appliances necessary for the securing of fresh and dried preparations of blood and the counting of the blood corpuscles were carried in boxes or trays. The animal was secured by its head, and, in rare cases, one hind foot was tied to forestall any injury to the one collecting the blood, whose entire attention had to be given to this work. If desired, a rectangular box or stall may be placed in each field into which the

animal may be led and secured. Or such a box may be placed under cover and then rainy weather will not interfere with the work.\*

(p. 198) In collecting the blood the hair is clipped and shaved away over an area 2 or 3 inches square on that region of the rump overlying the flaring hip bones (ilium), where the animal is most accessible for this work. The shaven skin is washed and rinsed with clear water and dried with absorbent cotton. To make the incision a spring lancet is used, resembling those advertised and figured in most catalogues of medical and veterinary instrument makers. The incision must pass through the depth of the skin in order that a sufficient flow of blood be secured. The depth to which the blade of the lancet penetrates may be regulated by a screw in the forked guard attached to the lancet. The lancet should be flamed in passing from one animal to another. The soap and razor should not be used on sick and healthy alike, for, although we have no positive evidence that the disease may be transmitted, either by these things or even by the lancet, such transmission is within the range of possibility.†

\* Such a box is best constructed as follows: Place three pieces of 2 by 4 studding,  $4\frac{1}{2}$  feet long, on the floor parallel to each other and 3 feet apart. Erect uprights also of 2 by 4 studding and 3 feet high, 15 inches from the ends of each horizontal piece, and brace securely from the outside. Within this framework build, by boarding up on the inside, a rectangular box 6 feet long, 3 feet high, and 2 feet wide, open at the top and one end. The front closed end of the box is hollowed out to a depth of 7 to 8 inches to receive the neck of the animal in the standing position, so that the head may extend over the end and be secured to a framework extending  $1\frac{1}{2}$  feet beyond the box and attached to the box 2 feet from the floor.

The whole framework must be very securely put together. The projection of the studding at the base with the braces on the outside serves to strengthen the box and to prevent its upsetting by the struggling of the animal. A bar can be slipped in behind the animal to keep it from backing out, and a rope or strap over the withers fastened to the sides of the box will prevent it from rearing forward.

† We give a specimen page of the figures obtained from counting the blood corpuscles as described above:

No. 218 (healthy control).—August 6, 1892, 10 a.m.: Temperature, 101.8; respiration, 64; pulse, 56; blood collected, 7.3 divisions.

(Toisons's fluid was used in this estimation. It consists of distilled water 160 cc., neutral glycerin 30 cc. (at 30°), sodium sulphate 8 grams, sodium chloride 1 gram, methyl violet .025 gram. It stains the white corpuscles so that both red and white may be counted in the same preparation.

*(Continued on following page)*

The number of red corpuscles in cattle (obtained from the counties around the District of Columbia) during health fluctuates more or less, as might be expected, but may be put down as six millions in a cubic millimeter. Seven millions in winter, and five millions in late summer and early autumn seems to be not uncommon. The number may be said to fluctuate, however, between four and one-half and eight millions, since these extremes are occasionally met with. The following counts from healthy animals will serve as illustrations:

(p. 199)	No. 109	No. 91
September 18, 1890.....	5,726,000	October 1, 1890..... 4,672,000
October 3, 1890.....	6,190,000	(Placed in infected field)
October 14, 1890.....	5,807,000	October 7, 1890..... 4,833,000
		October 30, 1890..... 4,670,000

(Continuation of footnote † from preceding page)

First row of squares:

8	12	9	13
13	11	10	14
12	13	13	10
14	19	8	13
12	7	10	10

$$61 + 62 + 50 + 60 = 233$$

$$\frac{463 \times 100 \times 4000 \times 10}{40 \times 7.3} = 6,342,465 \text{ red corpuscles.}$$

Second row:

8	14	7	13
11	9	10	8
15	13	13	13
8	8	15	17
12	13	9	14

$$54 + 57 + 54 + 65 = \frac{230}{463}$$

Seven white corpuscles in 400 squares.

$$\frac{7 \times 100 \times 4000 \times 10}{400 \times 7.3} = 9,589 \text{ white corpuscles.}$$

In counting 40 squares the various factors in the fraction above balance each other in such a manner that it is only necessary to divide the number of corpuscles (463) by the quantity of blood collected (7.3 divisions of melangeur instead of 10, the quantity usually collected). The first figure of the quotient gives millions. A similar simplification of the formula for the white corpuscles may be used.

## No. 143 (control animal)

September 29, 1890.....	6,261,900
October 8, 1890.....	6,835,000
October 25, 1890.....	6,500,000

In addition to these illustrations there was found a large number of figures relating to the number of red blood corpuscles of cattle in infected fields, but not yet diseased. The examination of the blood in 1891 was extended to many, and in 1892 to all, animals at the beginning of experiments, in order to get at the approximate normal for each animal, and also to make sure that the animals were in good health. Among the many cases which came under observation only one anaemic cow was found; that is, only one whose red corpuscles fell below four and a half millions. This animal (No. 136) was affected with some catarrhal discharges from the vagina. Her record was:

September 30, 1890.....	3,911,300
October 8, 1890.....	3,753,800
October 18, 1890.....	3,735,300

In one case tuberculosis, limited chiefly to the lymphatics, was discovered at the autopsy. Even in this animal, after three days of high temperature from Texas fever, the corpuscles still numbered 5,125,000. There could have been no anaemia, therefore, in spite of the tuberculosis.

The destruction of red corpuscles is the essential phenomenon of Texas fever, from which all the various pathological processes take their origin. Some illustrations will demonstrate these statements.

## No. 80

July 5, 1890—Beginning of exposure in infected field (Texas cattle)

Date	Number of corpuscles	Remarks
July 31.....	6,290,000	
August 4.....	5,052,000	
August 7.....	5,631,000	
August 23.....	5,422,000	
August 24.....	5,434,000	First high morning temperature on Aug. 24.
August 28—1 p.m.....	2,025,000	To all appearances in dying condition; killed.

## No. 129

July 5, 1890—Beginning of exposure in infected field (Texas cattle)

Date	Number of corpuscles	Remarks
August 11.....	6,123,000	
August 13.....	7,171,000	
August 16.....	5,370,000	
August 27.....	3,210,000	First high morning temperature Aug. 24.
August 29.....	1,675,000	Died at 8 p.m.

## No. 163

July 2, 1891—Beginning of exposure in infected field (North Carolina cattle)

Date	Number of corpuscles	Remarks
August 13.....	5,000,000	
August 24.....	3,368,800	Temperature last taken on 21st, then normal.
August 25.....	2,645,000	Killed.

These few examples will suffice to illustrate the rapid disappearance of red corpuscles from the circulating blood. They are by no means (p. 200) extreme cases, but stand for the average rate of disappearance in acute cases. This would be for No. 80 at the rate of about 1,000,000 corpuscles per cubic millimeter a day during the last three days; for No. 129 at the rate of 800,000, and for No. 163, 700,000. That this rate of destruction is very high becomes evident when we bear in mind that in No. 80 it represents the loss in twenty-four hours of one-sixth of all the red corpuscles usually circulating in the body. In the other cases it represents from one-seventh to one-eighth of the whole number.

In the mild nonfatal type the rate of destruction is lower.

In this animal, the loss which in an acute case would have taken place in four or five days occupied from seven to eight weeks. In these cases, however, other elements enter, such as the constant active production of new corpuscles which masks to a great degree the actual rate of disappearance. Moreover, the destruction seems to go on not regularly, but in jumps or paroxysms. Thus in the case before us there was a decrease of 1,912,000 from October 22 to October 25, but practically a standstill from October 25 to October 30, and so on.

September 8, 1890—Beginning of exposure in infected field (North Carolina cattle)

Date	Number of corpuscles	Remarks
<i>1890</i>		
September 20.....	6,844,000	
September 22.....	5,640,000	
September 29.....	5,307,000	
October 9.....	5,436,000	
October 22.....	4,666,000	
October 25.....	2,754,000	
October 30.....	2,720,000	
November 6.....	2,344,000	
November 8.....	1,984,000	
November 13.....	1,183,000	Lowest point reached.

Another fact of considerable interest brought out by the periodic estimates of the red corpuscles is the oscillation of the number up and down during the disease in some cases. It seems as if a period of destruction were followed by a period of regeneration, and this again by a period of destruction. This oscillation is occasionally traceable to the reappearance of the microparasite in the blood, as in one case, in which three different downward movements in the number of red corpuscles are associated with the reappearance of infected corpuscles. In other cases the microscope did not, during the downward movement, demonstrate the presence of the parasite, probably because such observations were often of one or two weeks apart. The supposition at the time was that such cases were getting well, and the tardy examination of the blood showed instead of the expected return to the normal another downward movement. A very good illustration of this oscillation is afforded by the following case, the result of the intravenous injection of blood from a sick native:

September 16, 1890.....	6,890,000
September 22, 1890.....	5,430,000
September 24, 1890.....	4,562,000
September 29, 1890.....	5,274,500
October 4, 1890.....	3,902,000

October 8, 1890.....	*5,983,600
October 22, 1890.....	4,333,000
November 4, 1890.....	5,586,000

\* This number is evidently too high as compared with the preceding, and must be explained by assuming other forces at work in concentrating the blood beside the mere regeneration.

(p. 201) It has been assumed above that the disappearance of the red corpuscles is chiefly due to their destruction. We have already seen that in the cases under observation there were very few hemorrhagic lesions which might for the time being reduce the number. The ticks can not be regarded at all as abstractors of blood in this stage.\* That they are largely destroyed within the body is shown (1) by the loss of haemoglobin through the kidneys, (2) by the overproduction of bile which is abnormal in the abundance of pigment flakes, and (3) by the actual observation of this destruction by the microparasite under the microscope.

#### THE REGENERATION OF RED BLOOD CORPUSCLES

*As determined by actual enumeration.*—Passing by, for the present, any further discussion of this interesting subject, let us turn to the regeneration of the red corpuscles. This, of course, varies in accordance with the vigor of the animal, its food, and the season of the year. It is, even under adverse circumstances, remarkably rapid and well adapted to occasion surprise.

The regeneration of corpuscles as indicated by the microscope is not in all cases indicated by the counting apparatus. That is to say, the regeneration may begin before the destruction has

\* The enlarged spleen, it is true, absorbs from  $1\frac{1}{2}$  to 3 pounds of red corpuscles, roughly speaking, since its enlargement is mainly due to an engorgement with them. If we regard the red corpuscles as constituting one-third of the weight of the blood, this quantity would correspond to  $4\frac{1}{2}$  to 9 pounds of blood. If we take the blood in cattle as one-thirteenth of the body weight (v. Limbeck, *Klinische Pathologie des Blutes*, S. 49) an animal weighing 800 pounds would carry 61.5 pounds of blood. The spleen would thus absorb the corpuscles of one-fifteenth to one-seventh of the entire blood and reduce the number of corpuscles in a cmm. one-third to one million. The capillary engorgement of the kidney, heart muscle, and perhaps other organs may account for some losses, but this is mainly due to infected corpuscles which may be regarded as destroyed. The above calculation, is of course, very approximate.



ceased, and if the latter process is the more active the count will show a loss, although the microscope may demonstrate the presence of a large number of new corpuscles. This actual regeneration, as indicated by abnormal forms, will be discussed farther on; here we will simply refer to the increase of the corpuscles as indicated by actual counting. A few illustrations will serve our purpose:

No. 64		No. 65	
September 9, 1890.....	3,154,000	November 4, 1889.....	1,720,000
September 16, 1890.....	4,575,000	December 2, 1889.....	3,463,000
September 29, 1890.....	4,869,000		
		No. 56 (Mild Type)	
		November 13, 1890.....	1,183,000
		November 15, 1890.....	1,534,000
		November 17, 1890.....	1,655,000
		November 21, 1890.....	2,615,000
		November 26, 1890.....	3,880,000
		December 2, 1890.....	4,706,000
		December 11, 1890.....	4,603,400
No. 102			
September 18, 1890.....	1,950,000		
October 4, 1890.....	2,682,700		
October 17, 1890.....	3,894,700		
November 6, 1890.....	5,120,000		

The activity of the regeneration is well brought out in No. 56, a large, vigorous ox. From November 17 to November 26 the red corpuscles appeared in the circulation at the rate of 250,000 per cubic millimeter per day. From November 26 to December 2, the rate of increase was about 140,000 a day. It is furthermore remarkable that in the case of a few calves under observation the corpuscles rose rapidly in number, although the animals did not thrive after the fever departed. This (p. 202) was likewise observed in some adults. The blood-forming function seems to go on independently of downward processes of other functions.

## No. 82

October 11, 1890.....	3,542,800
November 13, 1890.....	4,240,000
December 2, 1890.....	5,643,400

In this calf, the number of corpuscles steadily rose after the disease had passed away, in spite of growing weakness and diarrhea. On December 4 it was unable to get on its feet, so that it

had to be killed December 6. Opposed to these cases in which the blood-forming function asserts itself under difficulties, there are others in which the strain upon this function has been so severe that several phenomena appear.

The corpuscles may increase in number but not reach the full tide of the number present before disease until the following season. Or there may be a temporary standstill in the production of corpuscles when the number is still very low. In none of the cases in which the convalescence was followed with the corpuscle counter did the number remain below four millions after the end of three or four months.

*As determined by microscopical examination.*—The reproduction of new corpuscles as witnessed by microscopical examination presents a number of important phenomena. Taking it for granted for the present that we are able to detect newly formed corpuscles by certain peculiarities of form and staining which they possess during the more advanced stages of anaemia, we may lay down a few general propositions concerning this production. In the acute type of Texas fever, when the daily loss of corpuscles, amounts to from one-sixth to one-eighth of the normal number, there is observed little or no production of new corpuscles, until the number has fallen to one million or two millions, and the normal temperature has returned. Then an abundant crop of new forms is seen, even when the animal succumbs in the end. In the mild, non-fatal type, in which the destruction of red corpuscles goes on much more slowly, and in intervals, and in which there is but little fever and general disturbance of health, the production of new corpuscles begins at once and continues parallel with the destruction of older ones throughout the course of the disease. It is in such slowly progressive cases that the changes in the corpuscles accompanying their regeneration is best studied. Before proceeding to a description of these forms, so valuable in the diagnosis of Texas fever, a brief description of the methods employed is called for, since they are the same as those used in the important study of the microörganism or blood parasite of this disease.

The blood was examined in the fresh and in the dried condition.

The drop of blood as it oozed from the incision was received at once on a flamed platinum loop soldered into a glass rod like the ordinary bacteriological loops used for inoculating, etc. The platinum loop is simply brought in contact with the blood, and the drop placed on a clean glass slide and immediately covered with a cover glass and sealed with paraffin if the preparation is to be kept under observation for some time. The sealing is best done with a camel's hair brush dipped into melted paraffin. It is always desirable to have only a single layer of corpuscles in the preparation. To insure this there should be no speck of dust on slide or cover, and the quantity of blood taken must be small. This can be regulated by adjusting the size of the platinum loop. In the usual method of touching the drop of blood with the cover directly (p. 203) the quantity of blood can not be limited, and many preparations are subsequently found to contain too many corpuscles.

The preparation of dried blood requires much care. Without going into an extended discussion of the relative merits of different methods we give the one found most satisfactory and adopted in these investigations. It is most readily understood by referring to Fig. 2.

In A, a cover glass *cc* is held by a pair of forceps *b*, and has on its upper surface a drop of blood *a* placed there by a platinum loop. A second cover glass or "scraper" held by forceps is resting on the first with one edge, and is held at an angle of  $15^{\circ}$  to  $20^{\circ}$  to it. As shown in B the upper cover is drawn over the lower, and as its edge sweeps over it it spreads out the drop of blood in a thin layer. In rapid work the forceps may be dispensed with. The lower cover is held between thumb and forefinger of the left hand at *cc*, and steadied below with the tip of the middle finger, and the upper is firmly seized between thumb and forefinger of the right, where the blades of the forceps would rest. By using a pair of forceps, which may be adjusted by a clamp, the scraper may be fastened between the blades, and by rotating it its edges may serve to spread out three or four separate preparations. The scraper should be thick and its edges smooth in order to insure uniform distribution of the blood. It is needless to say

that this simple process is much superior to the barbarous one of placing two cover glasses together face to face in order to allow the blood to spread in a film between them, and then drawing them apart. Each corpuscle is thereby subjected to a long crushing process, whereas in the method before us this is entirely avoided. The thinness of the blood film depends upon several things, such as the condition of the cover as regards freedom from all grease, the size of the drop of blood, the regularity of the edge of the second cover or "scraper," and the angle at which it is held during the operation. The layer is not of even thickness over the entire cover glass, but is thinnest where the scraper has

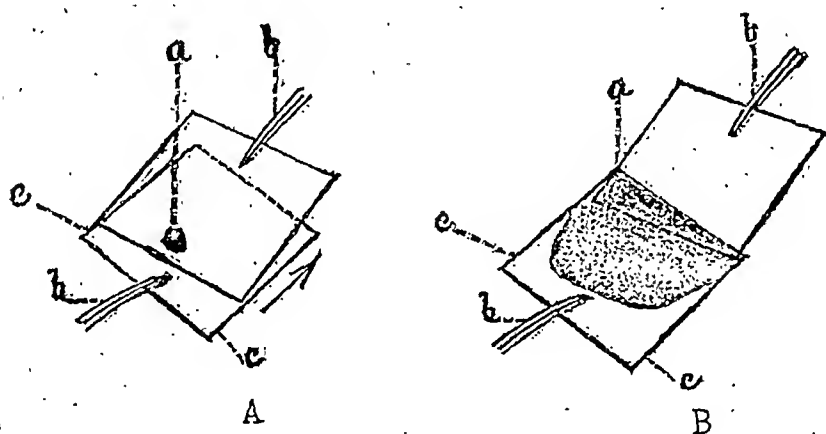


FIG. 2. METHOD OF PREPARING DRY BLOOD FILMS ON COVER GLASSES

begun its work, and densest where it has left off at the edge of the cover, as shown in the figure. This is no disadvantage, however, but rather an advantage, as it furnishes us with a layer of varying thickness which is of service, as will be pointed out farther on. The place where the scraper began, and where the layer is composed of isolated corpuscles or groups of contiguous ones, have dried so rapidly that they are in a state of perfect preservation. Every preparation has thus (p. 204) some spots where the corpuscles are thoroughly "fixed," even if, as a whole, it may have been a failure.

The essential condition of success in dry preparations of blood is to get the corpuscles into a dried state as soon as possible after

the blood is shed. For this reason it might seem desirable to eliminate the use of the loop and touch the exuding blood directly with the cover glass, as is frequently done in the study of human blood when the finger tip is pricked. But the circumstances are different in cattle. The prick is useless and an incision must be made. The surface of the skin is flat and a cover glass touched to the oozing blood may bring with it epithelial scales and other objectionable things from the skin accidentally touched, however much the latter may have been cleansed before-hand. Still, in rapid work, it is now and then of advantage to touch the oozing blood directly with the edge of the scraper. Not infrequently the quantity of blood is small and does not well out of the incision. A loop then becomes indispensable in lifting it out.\*

The dried films of blood, kept labeled in small pill boxes until used, are exposed in a dry-air oven to a temperature of 110°-120°C. for one and one-half to two hours. Drawing the covers through the Bunsen flame as for bacteriological preparations is liable to fail at any time from overheating or underheating, and is not to be recommended. When, for rapid work, this method must be used the cover glass should be drawn through the flame four times, each movement to occupy a second. Three movements are usually insufficient, for when the stain is applied the coloring matter of the corpuscles is dissolved out and the preparation is spoilt. When overheated the red corpuscles are apt to stain so deeply that any granules or parasites within them are hidden from view.†

The staining process used for the dried and heated cover-

\* More recent observations during the fall of 1892 have shown quite conclusively that cold rapidly destroys the form of red corpuscles. In fact it was impossible to prepare films out of doors in a temperature below 50°F.

† In place of a hot-air oven kept at the proper temperature by a thermo-regulator, the device of Ehrlich may be used. This consists of a Bunsen burner or a small kerosene stove and a strip of sheet copper laid over it. It is evident that at different distances from the source of heat the copper will be of different temperatures. By placing drops of water on it the place where the temperature is 100°C. can be approximately ascertained by the behavior of the water. The cover glasses are laid upon the sheet of copper for a certain length of time at a point corresponding roughly to 120°C.

glass preparations is very simple. The cover glass is either allowed to float on a filtered solution of Löffler's alkaline methylene blue or else the staining fluid is dropped upon the cover glass and allowed to remain from one and one-half to two minutes. It is thereupon washed in distilled water and dipped into a one-third per cent solution of acetic acid for an instant to remove any diffuse stain in the red corpuscles. Lastly the acid is washed away in distilled water.\* It is then ready for examination in water or for drying and mounting in xylol balsam. Care must be taken to make the action of the acetic acid solution momentary, otherwise the decolorization may go too far.

If we examine the blood of a mild autumnal type of fever every one, two, or three days, as described, certain phenomena appear regularly at certain stages of the anaemia. When the number of corpuscles has fallen to 3,000,000 a variable number of enlarged corpuscles appear. While the normal ones measure about 5 or 6  $\mu$  in diameter, the enlarged forms will be from 6 to 8  $\mu$  in diameter. This is the first change observable, (p. 205) and it appears only when, as stated, the number has fallen to one-half the normal. As the destruction goes on and the number sinks lower, the large cells become more numerous, but they at the same time grow thinner and more delicate. When the number is below two millions haematoblasts or nucleated red corpuscles begin to appear, and their number may be as high as 5 per cent of all corpuscles still in the circulation. It may also be noted at this stage that some of the large corpuscles show one or more small vacuoles in a cluster in the center of the corpuscle. These contain sometimes a barely visible ( $\times 1000$ ) particle in rapid dancing motion. These phenomena are all the result of the anaemia, as will be shown later, and have nothing to do with the microparasite. The variation in size of the red corpuscles is illustrated in Plate IV. Fig. 3, Plate V, Fig. 3, and on Plate IX.

When preparations of blood are dried and stained, another set of changes are observed which were hidden in the fresh preparations. These changes are limited to the enlarged cor-

\* If the film has been properly heated (not overheated), decolorizing is quite unnecessary.

puscles. When the number falls below 3,000,000 a few corpuscles are now seen among large numbers of others, whose disk is sprinkled over with a variable number of granules which stain deeply in the alkaline methylene blue.\* These granules vary in size. In some preparations of blood at this stage, they may be as large as  $0.5\mu$  in diameter, and there may be from 15 to 30 in a corpuscle. A prolonged observation of these granules has suggested the theory that their size depends largely on the rapidity with which the film of blood has been dried. In those portions of the layer which are thinnest and fixed instantly, only small granules are seen; that is, such as are, perhaps, not more than  $0.1$  in diameter. But in those portions of the layer in which the corpuscles are massed two or three deep, the large granules are found, if present at all. The immediate inference is that the stainable matter diffused through the corpuscle collects into larger nuclei if there is any time elapsing between the shedding and the drying of the blood. This time is longest in the dense portions of the film. (See Plate IV, Fig. 3, Plate V, Fig. 3 and Plate IX.) The granules in a cell are not all of the same size, although there is not much variation in this respect in the same corpuscle. There are cells with very fine granules, and cells with very coarse granules. Cells with granules of intermediate size are also found. The large granules are usually round, and resemble very closely micrococci, but the slight irregularity in form and size disposes one to reject at once the view that they may be micrococci. The large granules closely resemble one of the stages of the microparasite of Texas fever, as will be pointed out later on. The small granules do not appear round, but more angular, and even slightly rod-shaped. They are distributed quite uniformly over the disk, excepting in a few cases in which there was a central space free from them. These bodies stain, as nuclei and bacteria do, with basic aniline dyes, and they are not readily decolorized with acids. They are stained by haematoxylin and refuse to stain with Ehrlich's acid or neutrophile dyes.

The granular forms are characteristic of that stage of the

\* It should be borne in mind that under the conditions formulated above the normal red corpuscle does not retain the stain, either in the form of granules or diffusely.

anaemia in which the number of corpuscles stands between two and three millions. When it falls below 2,000,000 other peculiar forms appear. The enlarged corpuscles grow thinner and larger, more easily distorted when the drying is retarded, and when stained as above indicated, many of them show a diffuse, rather pale bluish coloration not easily removable (p. 206) by acetic acid. (Plate V, Fig. 1; Plate IX.) Some show instead of this diffuse coloration an aggregation of exceedingly minute granules which might easily give the impression of a diffuse stain. These types are not infrequently accompanied by haematoblasts. It must not be understood that the different stages of the anaemia are characterized by the exclusive presence of one or the other of these changed forms. The granular or "punctate" cells may be met with in the various stages of the anaemia. Likewise the diffusely stained forms are in a few cases encountered with the punctate forms before the anaemia has become advanced. But as a rule we meet first with the simply enlarged corpuscles, next with the "punctate" forms, and lastly with the diffusely stained or "tinted" forms and the haematoblasts.

It is not desirable to go into any details concerning the nature of these corpuscles, as this has already been done from the standpoint of general pathology in another publication where the literature is also taken into consideration.\* A few remarks are, however, in order as bearing upon an understanding of the disease before us. The various modified forms of red corpuscles, which we have been considering, are perhaps all embryonic or immature forms. They have been hastened into the circulation from their place of manufacture, the red marrow of the bones, to supply an urgent demand created by the destruction of vast numbers of red corpuscles by the Texas fever parasite. This demand grows more and more pressing as the number of corpuscles continues to go down, and consequently more and more immature forms are sent until the haematoblasts themselves, the progenitors of the red corpuscles, appear. The reasons for considering them embryonic or immature red corpuscles can not be entered into here. It must suffice to state that a comparative study of the embryonic

\* Theobald Smith: On changes in the red blood corpuscles in the pernicious anaemia of Texas cattle fever. Trans. Assoc. Amer. Physicians for 1891.



cells in the red marrow and of these modified corpuscles in the circulation shows them to be the same.

The stainable material in these new corpuscles may be some form of protoplasm imperfectly converted into the discoplasm of the adult red corpuscle. We have already presented the theory that the granules may be derived from the diffusely stained material by a condensation in the shed blood. This, of course, will demand special study. It is enticing to interpret, as has been done, the larger granules as fragments of the nucleus of the haematoblasts, but there are no observations directly supporting this view.\*

The same modified or embryonic forms of corpuscles appear in the acute type of Texas fever after the high temperature has disappeared and the stage of convalescence has begun. They disappear speedily from the circulation when the number of corpuscles again begins to rise. In fact they seem to disappear when the number has risen to 2.5 millions. Even when the regeneration does not go on quickly and the anaemia remains stationary for a time the punctate and tinted cells speedily disappear, while the simply enlarged corpuscles or macrocytes remain in the circulation, or rather are produced as such, until the number is above three millions, and they do not regularly disappear until the number is over four millions.

While there could be no reasonable doubt that the forms described as abnormal are immature red corpuscles, there was enough resemblance between the larger granules and the smaller stages of the parasite to make a crucial experiment necessary. It might likewise be claimed that the body to be presently described as the microörganism of Texas fever is nothing more than a phenomenon of embryonic or perhaps degenerated red corpuscles caused by some still unknown agency, which itself is the direct cause of the disease. It became therefore necessary to show that the parasites are not the result of the disease, and that in artificial anaemia they do not appear. To prove this, bleeding was resorted to—first upon a sheep, then upon a cow. The artificial

\* It is a curious fact that the granular, or "punctate" cells, have not been seen in the parenchyma of the various organs (spleen, liver, kidneys), although the diffusely stained or "tinted" cells are present.

anaemia brought about caused the various modifications described above to appear in the blood of both sheep and cow, but the various forms of the parasite did not show themselves at any time. These experiments are of sufficient importance to warrant their publication here. (See page 422.)

These two experiments show that the various changes which the red blood corpuscles undergo in Texas fever are solely the result of the (p. 208) rapid and enormous loss of red corpuscles. The enlargement of the corpuscles, the presence of stainable matter in them in the form of large and small granules, uniformly diffused, are phenomena accompanying severe loss of blood by whatever means this may have been brought about, and are indicative of an active regeneration of the blood elements. We are therefore justified in drawing a sharp line between these phenomena and those to be subsequently described as the Texas-fever parasite.

The white corpuscles of the blood did not obtrude themselves, so far as fluctuation in numbers is concerned, during the various stages of the acute and mild types of the disease. Hence quantitative determinations were not attempted until the latter part of the season of 1891, when Toison's fluid was used. Both red and white corpuscles were then estimated with little extra labor in the same preparation of blood. In all cases the 400 squares of the ruled cell of the Zeiss apparatus were counted. The number of leucocytes in these spaces is, however, so small (from 3 to 15) that we might anticipate only an approximate accuracy, unless we take the average estimate of three or four preparations. For this no time could be taken. Hence the figures as given in the appendix, based upon the method here described, can not be regarded as of much value.\* As far as they go, they indicate not very much fluctuation. Any unusual increase in numbers

\* The inefficiency of the method used has been commented upon recently by other investigators who have had occasion to use it. A melangeur is now specially prepared by Zeiss for the estimation of the white corpuscles, and constructed to give a one-tenth dilution of a considerably larger quantity of blood, in order to concentrate the white corpuscles. This was latterly tried, but found useless, since the capillary tube is so wide that it no longer retains the column of fluid by capillarity and the blood drops away before it can be mixed with the diluting fluid. We trust that this defect may be speedily remedied.

## Male lamb, 5 months old, still nursing—gross weight 65 pounds

Date	Number of red corpuscles in a cmm.*	Quantity of blood withdrawn from jugulars	Remarks
1890		grams	
June 17	11,500,000	336	
June 18	10,500,000	.....	Blood corpuscles not visibly altered.
June 19	9,200,000	406	Do.
June 20	6,500,000	.....	Do.
June 23	8,000,000	330	Many corpuscles enlarged (macrocytes). A few punctate cells.
June 25	7,500,000	.....	20-30 per cent corpuscles enlarged, about 10 per cent punctate.
June 27	8,200,000	160	The same number of macrocytes as before. Punctate cells have nearly disappeared.
July 1	7,500,000	546	Macrocytes as before. No punctate cells.
July 3	6,500,000	441	Do.
July 5	6,600,000	650	30-40 per cent macrocytes. 5-10 per cent punctate and tinted cells.†
July 7	5,600,000	.....	20-30 per cent punctate and tinted cells, the latter relatively increased.
July 10	7,100,000	.....	Macrocytes diminishing. Punctate and tinted cells absent.
July 15	8,900,000	.....	Corpuscles normal.
July 25	8,900,000	.....	Do.

\* This number was obtained before the bleeding in every case.

† See Plate IX, Figs. 1 and 2.

## Cow No. 168

Date	Number of red corpuscles in a cmm.*	Quantity of blood withdrawn from jugular	Remarks
1891		grams	
Aug. 3	6,762,500	2,268	Blood elements not visibly changed.
Aug. 4	4,988,700	2,325	Do.
Aug. 5	4,652,700	.....	Do.
Aug. 6	5,227,800	3,827	Do.
Aug. 7	3,820,000	4,251	Do.
Aug. 8	3,094,600	4,989	10 per cent macrocytes, 2-3 per cent punctate corpuscles.
Aug. 10	2,253,700	.....	20 per cent macrocytes, 15 per cent punctate corpuscles.
Aug. 11	2,143,000	.....	Same as yesterday.
Aug. 12	2,114,750	.....	Same as yesterday. (Plate IX, Figs. 3, 4).
Aug. 14	2,538,400	.....	Numerous macrocytes, 5 per cent punctate corpuscles.
Aug. 17	3,202,000	.....	Macrocytes as before. A few punctate corpuscles.
Aug. 22	3,200,000	.....	Macrocytes as before. No punctate corpuscles.
Aug. 29	4,325,000	.....	Only a few macrocytes.
Sept. 8	4,784,000	.....	Do.

\* This number was obtained before the bleeding in every case.

was not noted in the stained preparations of any case which came under observation. In some cases an abnormal crowding together of leucocytes was observed in dried preparations, which crowding must be regarded as having existed within the blood vessels, for there was no time for any massing together after the blood had left the vessels.

Whether the disease affects the different kinds of leucocytes either qualitatively or quantitatively has not entered into the scope of this investigation. It should be said, however, that in the stages of advanced anaemia, when haematoblasts are occasionally detected in the circulating blood, peculiar round bodies, which stain deeply and solidly with methylene blue, and which are a trifle smaller than red corpuscles, are frequently detected. A careful comparison of these with the nuclei of the haematoblasts makes it safe to regard the former as such nuclei which have been set free in the circulating blood.

#### THE CAUSATION OR ETIOLOGY OF TEXAS FEVER. TEXAS FEVER IS NOT CAUSED BY BACTERIA

We have thus far considered only the changes caused by the disease in the blood and the organs of infected cattle, and the manifestation of these changes during the life of the animal and after death. They are the concomitants and the resultants of certain causes at work in the body of the animal, and are to us interesting and important only in so far as they shed light upon the nature of these causes. And what are the causes at work in producing Texas fever? This problem has occupied the attention of a number of investigators since 1868. The general (p. 209) belief that Texas fever could be nothing else than an infectious disease due to the multiplication of some minute organism entering the body from without, led to a search for this microörganism by most of those who made this disease a special study. Dr. R. C. Stiles, of the Metropolitan Board, found in 1868 in the bile of Texas fever "preserved for analysis" minute vegetable organisms "in the form of spherical or irregular aggregations of micrococcus." From bile sent to Prof. Ernst Hallier, of Jena, Germany, this savant cultivated a mold (1, p. 1141-1150). It is

needless to go into the details of this investigation, for its methods are exploded and its results fantastical to say the least. Gamgee examined the blood of Texas fever with high powers, but found nothing unusual. Drs. John S. Billings and E. Curtis, of the Army, studied the blood with reference to the presence of cryptogamic growths at about the same time, but their efforts were fruitless.

Dr. D. E. Salmon, in 1883, described a diplococcus obtained from the spleen in cultures, but left its relation to the disease undecided (5, p. 13).

Dr. J. H. Detmers (5, p. 134) mentions the presence of bacilli and micrococci in the liver just after death, but none in the blood.

In a report published in 1888 Dr. Frank S. Billings claimed, somewhat pompously, to have discovered the "true germ" of Texas fever.\*

This germ is said to be like the germ of Billings' swine plague (hog cholera). It "has been found in the blood, the gall, the urine, the liver, spleen, and kidneys" of every diseased animal that was examined. It produces Texas fever in cattle when inoculated in "unquestionably pure cultivations."

This seems to be sufficient proof. In scientific research, however, especially when an important discovery is involved, it is incumbent upon the investigator to give at least to some extent the details of his experiments, so that others may form an opinion of their own as to whether the work was properly done and the conclusions or inferences warranted. Instead of a conscientious report of work done we find in this bulletin of 138 pages the same padding used in the swine-plague report of the same author. Quotations, criticisms, and discussions, mostly foreign to the

\* The announcement of this supposed discovery is entitled to quotation:

"Hence the germ of the Southern cattle plague has been discovered, and I think that I may be pardoned the egotism of claiming this to be the first occasion in American medicine that not only one but two germ diseases of animal life have been traced out and their origin placed upon an impregnable basis.

"The order of events seems to be reversing itself! The sun of original research, in disease, seems to be rising in the West instead of the East, so far as America is concerned. This honor does not belong to me alone," etc. (8, p. 72).

object of the report, together with an unwarranted dragging in of yellow fever, constitute the bulk of the text.

The germ of Texas fever as found by Billings stains at the ends. It grows on potato with a delicate straw color, which finally becomes a brick-red yellow. In the beef infusion gelatin tube it does not liquefy gelatin. These meager facts are not sufficient to distinguish this organism from a large group of bacteria living especially in the intestines of all domesticated animals. In fact, the few characters apply very well to the *bacillus coli communis*, a universal saprophyte in decomposing organic matter of intestinal origin, and one that has pathogenic properties with reference to smaller animals. This supposition is strengthened by the fact that Billings found in fresh and old manure bacteria not to be distinguished from the supposed Texas-fever germ.

As to the crucial test—the production of Texas fever by the inoculation of cattle with cultures of this germ—one case is reported. A black steer calf five months old presented four days after inoculation (p. 210) a temperature of  $42.5^{\circ}\text{C}$ . ( $106.5^{\circ}\text{F}$ .). The temperature remained high for two days, when the animal was killed for examination. A glance at the autopsy notes shows that there is nothing to prove that the disease was Texas fever. In the liver “each acinus was most beautifully demarcated by delicate lines of a bright yellow color, which represented the interacinus and distended gall ducts.” In Texas fever the bile injection is, as a rule, limited to the ultimate bile canaliculi within the acinus and rarely extends into the interlobular bile ducts. Was the bile stasis in the intralobular tissue actually seen under the microscope in this case? The important pathognomonic sign of Texas fever—haemoglobinuria—was absent. The evidence that this steer was suffering from Texas fever is therefore not sufficient by any means, although we do not wish to claim that it was not Texas fever. This latter disease may have been induced by contact with ticks, or by the presence of the Texas-fever parasite in the cultures originally introduced with blood or bits of tissue. The total absence of any experimental details as to what culture was used, how it was injected, where the

animals came from, etc., leaves us wholly in the dark as to the accuracy of the experiment.

These are all the facts of importance communicated by Billings in his report on the supposed bacterium of Texas fever.\* Even if the evidence to be adduced farther on were not diametrically opposed to them, the meagerness and vagueness of the statements made by him would prevent any candid, unbiased observer from accepting them without great reservation. As to some other theories presented by Billings in his report, we shall recur to them farther on.

In May, 1890, a bulletin on Texas fever was published by Dr. Paul Paquin, of the Missouri Experiment Station (9), which describes investigations conducted between September, 1888, and March, 1890. Paquin claims to have found a germ, but it is impossible to discover from the descriptions anything concerning the nature of this germ, excepting perhaps that it does not exist, and that a variety of microscopic things were seen in the debris of the blood, bile, and liver which were considered by the author without any supporting proof as to the Protean forms of a single organism. This kind of logic may suit disappointed observers, but it does not contribute anything to our knowledge of the subject. Moreover, in departing from established methods,† and in describing forms presumably existing which are wholly unlike any already recognized, the burden of proof rests upon the author and the work must be unusually well done to merit any attention. The conclusions reached by the author and presented on page 43 of the bulletin have none of them received even the

\* After the above was written an article by Billings on the etiology of Southern cattle plague (Texas fever) appeared in the *Journal of Comparative Medicine* for 1892, beginning with the July number. The remarks in the July and August numbers may be passed over without comment. In the September and October numbers is contained practically what has been stated above, largely drawn from his report. There is quoted in addition an experiment with cultures from ticks with which he claims to have produced Texas fever. While we are pleased to see that, since reading preliminary articles in the reports of the Secretary of Agriculture, Billings is now paying some attention to ticks, we must wholly dissent from his conclusions, which are practically the same as those reviewed in the text. The conclusions which we have drawn and those presented by Billings in these articles may be safely left to the judgment of future workers in this field.

† See p. 8, which describes the method of preserving tissues.

shadow of a proof in the text. That bacteria may be found in cases of Texas fever is unquestioned, but that they have anything whatever to do in producing the disease demands rigorous proof. It would be difficult therefore to analyze a (p. 211) report of experiments, however conscientiously pursued, in which the fundamental elements of scientific research—a careful record of such experiments and their details and sound logic in drawing conclusions from such experiments are at fault. We refer here only to the work involved in the study of the cause of the disease. The vaccination theory will be discussed farther on.

In the third annual report of the Arkansas Experiment Station (1890), Dr. R. R. Dinwiddie reports that in a large number of cultures on different media from three cases of Texas fever no bacteria developed. He also isolated bacteria from the intestines which proved negative when inoculated.

In our own work the first problem which naturally presented itself was to determine whether bacteria could be regarded as the cause of the disease. Hence the very first and some of the later cases were utilized for this purpose. As to the first postulate necessary to be fulfilled in demonstrating the cause of any infectious disease—to find with the microscope the bacterium or other organism in the body of the diseased animal—this failed utterly in all the cases examined. The thousands of cover-glass preparations of the blood, spleen, liver, kidneys, etc., examined fresh and stained, never showed any bacteria excepting when the animal had been dead for a number of hours. Animals killed in a dying condition were almost invariably free from bacteria. Those which succumbed in the night in midsummer contained usually large bacilli which are denominated post-mortem bacilli in the appendix, and which are familiar to every worker in bacteriology. They are specially abundant in the carcasses of large animals, from the pig up, which have been dead some time; probably because a large carcass remains warmer and more thoroughly deoxidized than a small one, and thus becomes a good medium for this anaerobic bacillus to flourish in. These bacilli do not grow in ordinary culture tubes, excepting perhaps very feebly in the bottom of bouillon tubes and in impure cultures on



agar-agar. They are somewhat broader than anthrax bacilli, have rounded extremities and usually occur single. They stain readily and deeply in all aniline dyes. The mention of this familiar intercurrent bacillus might have been passed over were it not that observers who have described bacteria in connection with Texas fever may have occasionally mistaken this as the cause (9, p. 43, third conclusion).

As to the cultivation of any bacteria from the blood and tissues in Texas fever, the results are equally negative. Special attention was paid to this phase of the problem in 1888. In the appendix will be found a brief statement of this work under the first six cases, and after the sixth a summary of the results obtained with a bacterium which appeared a number of times in the cultures. That it was the ordinary *bacillus coli communis* of the intestines which had found its way into the liver and thence into other organs there can be no doubt, for subsequent comparisons with *bacillus coli* from the intestines of healthy cattle proved them to be identical. It should also be remembered that this bacillus was present in exceedingly small numbers, as will be seen from the quantity of tissue or fluid used for inoculating the various culture media, and from the fact that they were never seen in cover-glass preparations. A large series of cultures were also made from several cases of the disease in 1889 and 1890 with equally negative results. In most cases the culture remained absolutely sterile. In some a few cultures developed, the contents of which were explainable either as contaminations or as coming from an animal in which frequent (p. 212) skin incisions in the last stages of the disease may have led to the introduction of a few bacteria into the circulation. The results obtained from cattle infected by Texan animals were as negative as those from North Carolina cattle. Cultures have thus far been made from four different outbreaks, and the blood and the tissues have been examined microscopically from as many more.

We are, therefore, ready to admit that there are no bacteria in the blood and tissues of animals suffering with Texas fever, excepting occasional individuals which probably enter the circulation from the intestines by way of the disintegrated liver. But

may there not be bacteria living only in the intestinal tract which send their toxic products into the circulation and thus cause disease? This hypothesis might be attractive to those who will insist on bacteria as the cause of Texas fever, but there are no facts to support it, and in view of the more definite results obtained by us its discussion is useless.

#### THE MICROÖRGANISM OF TEXAS FEVER

(*Pyrosoma bigeminum*, n. sp.\*)

Although Texas fever is essentially a blood disease, and only secondarily affects the spleen, liver, and kidneys, most observers have failed to recognize this fact. R. C. Stiles (1) was the earliest and the only observer who laid any stress upon the changed condition of the blood corpuscles. He says: "The red blood corpuscles when examined immediately after removal from the body were shriveled and crenated without artificial provocation. . . . In one case many of the disks appeared to have lost a portion of their substance, as if a circular piece had been punched out, the addition of water failing to restore the disk to completeness." There can be but little doubt that Stiles saw at that time the microörganism of Texas fever, without, of course, recognizing it, since this description applies very closely to the appearance of red corpuscles infected by this microparasite when the blood and the parenchyma of liver, spleen, and kidneys are examined fresh soon after death. Other observers have examined the blood, but have seen nothing unusual.

In 1888 during the examination of portions of the organs of a few cases, the destruction of the red corpuscles seemed to be the one prime phenomenon of the disease. The large quantity of haemoglobin in the urine, and the peculiar condition of the liver and the bile indicative of hyper-secretion could not but lead to the hypothesis that there was some destructive agency at work in the blood. R. C. Stiles in 1868 assumed the liver to be the primary focus of the disease, and believed that the alteration of

\* For the preliminary announcement of the discovery of this micro-organism see the Annual Report of the Secretary of Agriculture for 1889, the Medical News for December 4, 1889, or the Proceedings of the American Public Health Association for 1889.

the blood elements was due to the absorption of bile from the liver into the circulation. This inference from the observed pathological phenomena is erroneous, for the liver is doing too much work rather than not enough, and the destruction of blood corpuscles goes on very early in the disease. The outcome of the work in 1888 was the formulation of several theories as to how the blood corpuscles came to their destruction:

(1) There may be organisms in the blood which by the production of toxic products act directly on the corpuscles.

(2) There may be some toxic substance in the digestive tract which (p. 213) is absorbed into the blood and causes a dissolution of the red corpuscles. This substance may be the product of specific bacteria multiplying only in the digestive tract.

(3) There may be microparasites which invade the red corpuscles in a manner similar to those of malaria, and which by their growth disintegrate the containing corpuscle.

The first hypothesis was soon made improbable by the absence of any demonstrable organisms in the parenchyma of the various organs which are abundantly supplied with blood, such as the liver, spleen, and kidneys. To test the second the contents of the digestive tract, more particularly the small intestine, were carefully examined microscopically in 1888 and many plates and rolls of gelatin were made with the intestinal contents without bringing to light any other than the ordinary intestinal bacteria. It is true that this method was merely preliminary, and would have been followed by more exhaustive bacteriological studies of the digestive tract had not the third hypothesis furnished the clew. This, however, could not be tested in 1888, since no living animals were accessible, and the results of the study of the blood elements could not be considered reliable when obtained only from the organs of animals dead twenty-four hours, or even longer. In the very first case which succumbed on the experiment station at Washington, in 1889, certain microorganisms were found within the red corpuscles which will now claim our attention. It should be said, however, that these bodies were noticed in the spleen of a case as early as 1886.

PECULIAR BODIES FOUND IN THE RED CORPUSCLES OF  
HEALTHY CATTLE

In endeavoring to prove the existence of specific parasites in the blood as causes of disease it becomes necessary to prove their absence during health. A large series of microscopic observations have been made upon the blood of cattle which were not infected, as well as upon those which were infected, before the disease had appeared and after it had passed away. In a preceding chapter we have treated of the number of red corpuscles in health and in Texas fever, also the changes which they undergo in this disease and the methods to be used in studying them. These methods apply in the study of the microorganism, and the reader is referred to them. The red corpuscles of cattle retain their form pretty well when examined in the fresh condition. After a time small conical protrusions form on them as they shrink and shrivel, and the stramonium forms begin to appear.

In 1890 certain minute bodies were first observed within red corpuscles of cattle in health. They are present in variable numbers. In some cases they are not found even after prolonged examination of cover-glass preparations (apochrom. 2 mm. oc. 4 or 8). In some a few may be seen in a single field. In several cases as many as 10 per cent of the corpuscles contained them. They may appear as barely visible points with a bright luster. Whether this brightness is a resultant of the color of the body itself and that of the corpuscle within which it is lodged it is impossible to find out. Suffice it to state that as we look into the microscope at a corpuscle containing one of these bodies it appears as a bright, almost golden speck. These bodies are not all of the same size and form, although their minuteness makes it impossible to express differences in figures. They range in size from mere specks to quite appreciable coccus-like bodies. Frequently a rod-like form (p. 214) with a central constriction, reminding one of diplo-bacteria, appears. It may be that the rod-like forms are observed as round bodies when standing on end within the corpuscle. In general they are rarely  $0.5 \mu$  large, usually much smaller. In the table of the appendix they are

indicated provisionally as bright bodies. \* Plate VI, Fig. 9 gives an approximate idea of the relative size of these bodies. The third and the fourth corpuscle contain bodies which are much too thick, however.

Another interesting phenomenon of these bodies is their occasional motility. Many change their place within the corpuscle. When first detected the speck is usually situated at the periphery of the corpuscle. When watched closely for a few minutes it may be seen to move toward the center of the corpuscle, then back again toward the periphery. Then the movement may be along the periphery for a distance, succeeded perhaps by a movement across the entire corpuscle. The smallness of these bodies does not allow us to state whether this movement is passive and due to currents within the corpuscle, or whether it is the active, spontaneous movement of a living organism. There are, however, cases in which it is difficult not to accept the view that the movement belongs to a living body. The warm stage seems to accelerate these movements, but since heat is also likely to cause disturbance of the fluid within the corpuscle, this acceleration does not add to the proof that we have organisms before us. Fig. 10, on Plate VI, shows the path of one of these motile bodies. They do not reappear in dried and stained preparations, which means that they do not stain.

It has already been stated that these bright specks are present in the red corpuscles of healthy cattle. They are found in all seasons of the year and in most animals examined, in Southern (North Carolina and Texas) as well as native cattle. Besides these bright bodies, many of which are constantly changing their places within the corpuscle, there are occasionally seen in the fresh blood, both in health and during the fever period of this disease, bright rod-like bodies within corpuscles, which do not change their place. They lie usually at the edge of a paler area within the corpuscle, and the impression is conveyed that they are crystals derived from the haemoglobin of the adjacent pale spot. There are from two to four of these minute rods in the affected corpuscles.

In addition to these intraglobular bodies present in healthy

blood, certain forms are now and then seen in dried preparations stained in methylene blue which might be mistaken for Texas fever parasites. They are round, deeply stained coccus-like bodies situated quite near the periphery of the corpuscle and about one to two  $\mu$  in diameter. There is never more than one in a cell. They differ from the intraglobular parasite by a deep blue stain and by the compact, round form. They are probably remnants of the nucleus of the ancestor of the corpuscle—the haematoblast.\*

(p. 215) THE MICROÖRGANISM IN THE ACUTE TYPE OF TEXAS FEVER

In describing the microparasite of Texas fever we shall describe the various forms and stages as they are met with in actual examinations first, and then construct its life history as far as that is possible from the recorded facts.

*In fresh blood of the acute disease during life.*—When blood is drawn from the skin during the fever and examined at once with high powers (500 to 1,000 diameters, Zeiss apochrom., 2 mm., oculars 4 and 8) certain corpuscles will be found containing two pale bodies of a pyriform outline. One end of each body is round and the body tapers gradually to a point at the other. They vary somewhat in size in different cases, but the two bodies in the same corpuscle are as a rule of the same size. They are

\* The interpretation of appearances in the field of the microscope is frequently beset with difficulties, and certain foreign bodies are likely to intrude and give rise to false impressions. To those accustomed to the examination of the blood elements this is not likely to happen, but to the beginner in this work certain suggestions will not be superfluous. In preparations of fresh blood from cattle a large number of very minute refracting spherical bodies about as large as the earlier stages of the Texas fever parasite are frequently found in all parts of the preparations. They may be attached to the disks of many corpuscles, and appear like intraglobular bodies. Their presence in other parts of the field free from corpuscles, as well as careful focusing, shows them to be foreign bodies. Prolonged observation has led to the inference that they are derived from the fat in the sebaceous follicles of the skin, because they have been occasionally encountered in masses on the slide. The incision perhaps dislocates such masses and the blood carries them out.

In stained preparations bluish spots are not infrequently found on red corpuscles which might be mistaken for parasites. They are nothing more than blood plates which have attached themselves during the drying of the film to the corpuscles. In general it may be said that such misinterpretations will not occur after the various stages of the microparasite have been once recognized.

from 2 to 4  $\mu$  in length and 1.5 to 2  $\mu$  in width at the widest portion. (Plate VI, Figs. 4, 5, 6.) Their tapering ends are directed toward each other and usually close together; their rounded broad ends may occupy various positions with reference to each other. They may be seen together with the axes of the bodies nearly parallel, or they may be far apart, the axes forming a straight line. (Plate V, Fig. 2.) The bodies themselves have a homogeneous, pale appearance contrasting markedly with the inclosing red corpuscles from which they are sharply outlined. There is no differentiation into peripheral and central zone, no granular appearance of the body. Several slight variations in the appearance of these bodies at different times have been noted. The smaller forms are as a rule homogeneous; the larger forms are very frequently observed to be provided, in the rounded end of the pyriform body, with a very minute spherical body probably not more than 0.1 to 0.2  $\mu$  in diameter, which contrasts dark with the body itself. In several cases it manifested a brilliant luster with very high powers. (Plate VI, Figs. 4, 5; Plate VIII, Figs. 4, 5.) In the largest pyriform bodies there was seen in the center of the enlarged end a somewhat larger round or oval body which seemed to take the place of the smaller body or else be associated with it. This second body was from 0.5 to 1  $\mu$  in diameter. It changed its appearance with the focus. At a low position of the objective the parasite appeared dark with a light round spot in the enlarged end. At a higher position of the objective the inner body appeared dark, inclosed in the lighter pyriform outline. One or both of these bodies were observed in some of those forms undergoing amoeboid changes.

A question of considerable interest to be discussed farther on is the relation of these two pyriform bodies to each other in the same corpuscle. Any direct mutual connection of their tapering ends is not demonstrable in the fresh preparation.

When exposed to a temperature of 35° to 42°C. on the warm stage\* (p. 216) some of these bodies, by no means all, exhibited

\* Pfeiffer's warm stage as constructed by C. Zeiss was used. The entire microscope is enclosed in the box (with the exception of ocular and adjustment screws). The heat is communicated to the heavy iron bottom of the box and thence to the air and the micro-

changes of outline. These may go on continuously in some bodies, in others quite slowly. The motion most frequently exhibited consists not so much of a thrusting out and withdrawing of pseudopodia as of a continual recasting of the general outline of the body as we find it for example in the leucocytes of mammalian blood. (Plate VIII, Figs. 1, 2, 3.) The changes of form may go on so continuously and so rapidly that it is not possible to sketch them all, as some escape observation during the sketching. The motion described does not of necessity require the stimulus of heat. During the past summer the same continuous rapid changes were observed in preparations of blood, sealed with paraffin, at 75° and at 85°F. In the former case the slide had been prepared at 10:45 a.m. The motion was still noticeable at 3:10 p.m., when the observation was discontinued. In the latter case the observation was discontinued six hours after the drawing of the blood, although the motion had not yet ceased. The sparseness of the microparasite in the blood makes it impossible to state definitely whether this amoeboid motion belongs to a certain stage of its life. On the whole the observations tend toward the inference that the pyriform bodies do not change their form, and that the motion belongs to a younger stage. It should likewise be stated that the amoeboid bodies observed were apparently single within the corpuscle.

If dried cover-glass films, heated, stained in alkaline methylene blue and decolorized, as described, be examined in water or balsam—preferably the former—it will be found that the forms described have become stained. The staining, however, is more feeble than in those microparasites found in the internal organs after death. It is limited usually to a zone on the periphery of the body, the center being feebly blue or entirely free from coloring matter. (Plate V, Fig. 2, 3d; Plate VI, Fig. 7.) In the latter condition it has been observed that these circulating forms

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scope stand which rests upon it. The drawback to this apparatus is the large amount of heat which is stored in the iron base and which may cause the temperature of the stand to rise faster than that of the surrounding air. As these observations upon the fresh blood had to be made mainly at the experiment station with no gas at hand, the heat was applied with an alcohol lamp and the thermometer carefully watched.



have a peculiar luster, as if they possessed (in the dried and stained condition) feebly refracting powers. Other basic aniline dyes, such as methyl violet and gentian violet, are equally applicable. Fuchsin stains the organism, but also affects the containing corpuscle, so that the pictures obtained with it are not satisfactory. Haematoxylin likewise stains the organism fairly well. In general the clearest, most distinct pictures have been obtained with Löffler's alkaline methylene blue.

The intraglobular parasites found in the acute stage are not all pyriform and paired. In fact a considerable number as seen in stained preparations are somewhat irregular in outline and single. There are probably the bodies which were undergoing amoeboid changes when they were dried in the film on the cover glass. Some of these irregular forms are shown on Plate V, Fig. 3.

The corpuscle which contains such a pair of microparasites has fully one-fourth of its area occupied by them. That this invasion is detrimental to the corpuscle is easily understood. In preparations of fresh blood the corpuscle has a peculiar appearance. Its margin is irregularly notched and creased, the border may be beset with projecting spine-like processes and its color may be darker than that of the normal corpuscle. It has, to use a fitting expression, a wrecked appearance. This change is more marked in some cases than in others. Such corpuscles have lost their characteristic flexibility. They retain their disk-like form, even after normal corpuscles have become shriveled and folded in preparations kept under observation for some time.

The number of infected corpuscles circulating in the blood during the high fever is usually quite small. It is difficult to make an approximate (p. 217) estimate without careful counting. Probably one or two in a single field of the 2-mm. objective, or from half to 1 per cent, is near the truth in most cases. In some, however, a long search is necessary before one is brought into view. When the number grows larger death is not far distant, and may be expected within twenty-four hours. Toward the fatal termination, there may be from 5 to 10 per cent of the corpuscles with the pyriform parasites present. Fig. 2 on Plate V is an illustration of a group of such infected corpuscles taken

from the blood on the last day. Very rarely large numbers of parasites may be present and yet the animal recover. The only case of this kind is No. 49, in which haemoglobinuria appeared at the same time. When present in considerable numbers in the blood the infected corpuscles usually appear in groups in the field of the microscope, as is shown in the figure referred to, and not uniformly distributed.

When the fever has subsided and the number of red corpuscles has been greatly diminished, the parasites disappear quite rapidly from the blood. In fact, the reduction of temperature usually coincides with the more or less complete disappearance of the infected corpuscles, and their place is then taken by the large number of embryonic corpuscles which begin to replace the losses. An occasional infected corpuscle may be detected for some days or even a week after recovery has set in. But they are so scarce that their detection is more of an accident. After the subsidence of the fever, when there is a general sinking of the vital powers, leading to death, the parasites may linger on in the blood in small numbers or they may disappear as in recovering cases.

*Parasites in internal organs.*—With only 1 or 2 per cent, or even 10 per cent, of infected corpuscles in the circulating fluid, it would be difficult to account for the enormous daily losses of blood corpuscles in the acute fever. The difficulty is cleared up by sacrificing an animal in the earlier days of the fever and examining the internal organs for infected corpuscles. Large numbers of parasites are found within corpuscles in the capillary blood of congested areas, such as those of the heart muscle and of the omentum. In the latter membrane there are delicate fringes containing capillaries which may be placed entire on a slide and examined with the highest objectives. In such capillaries in the fresh condition, with perhaps a little iodized serum added, the pale intraglobular parasite may be seen quite distinctly. When such fringes are torn and crushed on cover glasses and dried films prepared and stained, the large number of parasites is at once revealed. (Plate VI, Fig. 1.) The same may be said of the muscular walls of the heart. In these the smaller

vessels are seen by the unaided eye to be engorged, and in sections the capillary network is found in the same condition. (Plate VI, Fig. 2; Plate VII, Fig. 1.) If a piece of such muscular tissue be compressed and dried films made from the blood squeezed out, an unusually large number of infected corpuscles will be found.\* These statements are best illustrated by a case:

No. 163 was killed August 25, 1891, when her temperature was 107. On the morning of August 21 her temperature was still normal (101.6). It was not taken until August 24, when it was 106.8. If we assume that the first high morning temperature occurred August 22, she was killed at the end of the third day of continued fever. Even at this time there had been great losses in blood corpuscles.

August 13.....	5,000,000 in a cmm.
August 24.....	3,338,800 in a cmm.
August 25.....	2,645,000 in a cmm.

Before she was killed there were 2 to 3 per cent of infected corpuscles in the circulating blood. In the internal organs there were found in cover-glass preparations made at the autopsy—

- In blood from skeletal muscles very few infected corpuscles.
- In blood from the right heart very few infected corpuscles.
- In blood from marrow of sixth rib very few infected corpuscles.
- In blood from the left heart 2 to 3 per cent infected corpuscles.
- In blood from lung tissue 2 to 3 per cent infected corpuscles.
- In spleen pulp 5 per cent infected corpuscles.
- In liver tissue 10 to 20 per cent infected corpuscles.
- In kidney tissue 10 to 20 per cent infected corpuscles.
- In hyperaemic fringes of omentum 50 per cent infected corpuscles.
- In heart muscle 50 per cent and many free parasites.

This distribution of the infected corpuscles and their localization in the capillaries will receive more attention later (Plate VII). Meanwhile we simply wish to point out that, while only a few parasites may circulate in the blood, the infection may reach 50 and even more per cent in the internal organs. The parasites

\* In such preparations, the falciform bodies of *sarcosporidia* cysts are frequently present, especially when the preparation is from a cow over 5 years old.

as they appear in the capillaries differ somewhat in form from those in the circulating blood. Their form may be best seen in dried and stained preparations of the capillary blood of the heart muscle. (Plate IV, Fig. 5.) They appear slightly smaller than in the circulating blood and the outline of many is spindle shaped or fusiform, i.e., tapering at both ends. (Plate VI, Fig. 1.) In this stage, which is probably one of active growth, they stain very well. The stain is deeper in that half of the body directed towards its mate in the same corpuscle. Distinctly pyriform bodies are also present, and these as a rule take the stain quite uniformly. In preparations of fresh blood from the same source no differences are observed except an absence of the minute nuclear (?) body in this stage. It may be that we have to deal with forms younger than those which circulate in the blood. (See Fig. 3.)

Changes of form of an amoeboid nature have already been referred to. If the organs of an animal which has been dead for five or six hours be examined it will be found that all the intraglobular parasites have a roundish form, and that distinctly fusiform or pyriform bodies are to be seen only occasionally in preparations from the heart muscle. (Plate V, Fig. 1.) The inference is that the microorganisms have assumed the spherical form under the adverse conditions presented by the death of the host. Similar changes are observed after a time on the warm stage. The pyriform and spindle-shaped bodies which have been thus far described may therefore escape the attention of those who study the blood and the organs after death only. The blood is rarely in a condition to be examined after death, because the corpuscles lose their disk-like form very speedily. In the various organs they are preserved fairly well even for hours after death.

The relative number of infected corpuscles in the internal organs demands some attention. This was estimated approximately in dried and stained cover-glass preparations after examining a large number of fields. The cover-glass films were made like those from the blood. A smooth, fresh incision was made into the organ, the cover glass gently drawn over the cut surface, and the film allowed to dry. This gave thin and uni-

form films. The very soft and partly disintegrated spleen pulp required some other procedure. A little of the pulp was scraped up with the edge of one cover glass and then quickly drawn over another, as in the preparation of blood films. This usually insured layers thin enough for microscopic examination.

A comparison of the various cases which have been examined shows (p. 219) that there is a considerable variation in the number of infected corpuscles found in the body after death, according as the animal succumbed in the fever stage, or after the number of red corpuscles had been greatly reduced and the fever had passed away. In the former case the infection is very extensive, as the following illustrations show:

No. 128 (Texas infection)

Blood from skin and heart, 10 to 20 per cent corpuscles contain parasites.

Blood from spleen, 10 to 20 per cent corpuscles contain parasites.

Blood from liver, 40 to 50 per cent corpuscles contain parasites.

Blood from kidneys, 80 to 90 per cent corpuscles contain parasites.

No. 130 (North Carolina infection)

(Number of corpuscles two days before death, 3,922,000.)

Marrow of rib, 5 per cent of corpuscles contain parasites.

Blood from skin and heart, 10 to 15 per cent corpuscles contain parasites.

Blood from spleen, 10 to 20 per cent of corpuscles contain parasites.

Blood from liver, 20 to 30 per cent of corpuscles contain parasites.

Blood from kidneys, 60 to 80 per cent of corpuscles contain parasites.

Capillary blood from heart muscle and omentum, 50 per cent of corpuscles contain parasites.

In those cases in which the number of corpuscles has fallen quite low, i.e., below 2,000,000 before death, the number of such as are infected must necessarily be low, because there are so few corpuscles remaining. Of these the majority may be embryonic or new forms.

No. 184. (Temperature on the last day, 103.2; number of corpuscles, 1,822,500.)

Blood (subcutaneous and from heart cavities) contains  $\frac{1}{2}$  to 1 per cent infected corpuscles.

Spleen, 2 to 3 per cent infected corpuscles.

Kidney and liver, 20 to 30 per cent infected corpuscles.

Heart muscle, 10 to 15 per cent infected corpuscles.

No. 95. (Chronic case. Infection first detected August 7; killed in dying condition August 25. Blood corpuscles 1,858,800.)

Blood before death contains 5 per cent infected corpuscles.

Spleen contains 2 per cent infected corpuscles.

Kidney and liver contain 5 per cent infected corpuscles. The former organ also contains many free parasites.

These illustrations may suffice here to demonstrate the variable number of infected corpuscles found at the autopsy. As to their distribution over the body, something has already been stated. They are very abundant, as determined thus far, in the capillary blood of the heart muscle, but quite rare in that of the skeletal muscles. Of the internal organs the kidneys usually contain the largest number; not infrequently from 50 to 80 per cent of all the corpuscles are infected. (Plate IV, Fig. 4; Plate VII, Fig. 2.) Next comes the liver, then the spleen. In spite of the fact that this organ is loaded by several times its own weight with red corpuscles rarely more than one-tenth contain parasites. Infected corpuscles have been found in great abundance in the capillaries of the choroid plexus of the lateral ventricles of the brain and in the vessels of the pia and the brain substance. They have also been detected in the capillaries of the intestinal mucosa.

*Freed parasites.*—In view of such enormous destruction of red corpuscles the question naturally arises whether freed forms of the parasite are not regularly observed. In the circulating blood none have been seen. In the preparations from the heart muscle of various cases there are seen a large number of free bodies in pairs as they are found in the corpuscle. Unstained, they float in pairs in the blood under the (p. 220) cover glass, sometimes as pyriform, sometimes as round bodies. (Plate VI, Fig. 8.) They have a homogeneous grayish appearance. Whether there is at

this time any organic connection between the pair by their tapering ends or simply by invisible remnants of the once enveloping corpuscle has not yet been made out. In some instances the shadowy outline of the corpuscle may still be seen around them. Motion has not been observed. The only other organs in which free bodies are found are the kidneys. (Plate VI, Fig. 3.) These organs are generally filled with infected corpuscles. In the fever stage we may find in dried films and in stained sections very few corpuscles which do not contain a pair of parasites. When the number of corpuscles has fallen quite low before death and the destruction has practically ceased there may still be found, in dried and stained films of the parenchyma, immense numbers of free parasites. They appear as roundish coccus-like bodies grouped in pairs and varying slightly in size, never as pyriform or fusiform bodies. To a casual observer they might appear as coarse granulations of broken-down cells and cell nuclei, but a little study and comparison of different cases soon dispels this view.

#### THE MICROÖRGANISM IN THE MILD TYPE OF TEXAS FEVER

We have thus far considered only those forms of the parasite found in the acute type of the fever. This type will now be understood to be one in which there is a very rapid multiplication of the microparasite in the blood vessels corresponding to an equally rapid disappearance of the red corpuscles. The forms of the microparasite are pyriform and fusiform bodies chiefly intraglobular, occasionally free. The post-mortem forms are roundish. In size the pyriform bodies are quite large, and the question arises, are there any smaller forms to be found? For these we must turn to the mild (usually autumnal) cases of the disease. It is an interesting fact that these cases are characterized by the presence of the smaller stages of the parasite. While the pyriform bodies are not entirely absent, they are very rare. In the acute type only the latter and not the former are seen.

In the mild type we have from 5 to 50 per cent of the red corpuscles in the circulating blood infected for a period of from one to five weeks. In the acute type, on the other hand, the

circulating blood contains usually from one-half to 2 per cent of infected corpuscles; 10 to 15 per cent is a rare occurrence, usually just before death. In the fresh preparations of blood this small stage of the parasite is as a rule invisible. Rarely we may observe it on the very border of the corpuscle as a round pale spot about  $0.5\ \mu$  in diameter, which does not change its place. When dried films of blood are stained in alkaline methylene blue the parasites appear as round coccus-like bodies from  $0.2$  to  $0.5\mu$  in diameter and situated within the corpuscle on its border. They sometimes appear as if situated on the border, but outside of the corpuscle. As a rule only one is found in a corpuscle. (Plate IV, Figs. 1, 2, 3.) In many cases a division of the coccus-like body into two could be clearly made out. The separation was noticeable as a paler line and a constriction at either end similar to the division of certain micrococci. This division usually appeared in all bodies of a preparation from one case, but could not be noticed in any preparation of perhaps the next case.

These bodies stain as well as the larger pyriform bodies in basic aniline dyes and in haematoxylin. They do not stain in acid dyes, such as eosin or in Ehrlich's dye for neutrophile granules. When this stain is employed (p. 221) the corpuscles, beautifully tinted, show a small round unstained spot where the parasite is situated. When the dried films are treated with dilute acetic acid the corpuscles fade out, while these coccus-like bodies remain behind and stand out prominently.

It has already been stated that these bodies are characteristic of the mild, autumnal type of the disease. A glance at the appendix will show how numerous these cases may be. This stage of the parasite is there indicated provisionally as "peripheral bodies" or "peripheral coccus-like bodies". A more careful examination of these cases will reveal three groups:

- (1) Animals exposed to Texas fever late in the season (October and November).

- (2) Animals which have passed through an acute attack earlier in the summer (second attack or relapse in October and November).



(3) Animals which contract a mild disease during or previous to the season of the acute disease.

In the first group the disease is mild and may pass unnoticed. The corpuscles with peripheral bodies appear in the blood as the number of corpuscles begins to fall, and disappear when it again begins to rise. Rarely a corpuscle with a pair of large pyriform bodies is detected.

In the second group the phenomena are the same.

To the third group belong a few cases which showed a blood infection several weeks before the fever appeared among all the susceptible animals in the infected field. In two cases the infection was at first by peripheral coccus-like bodies. This, after a week's time, developed into an acute fatal infection, in which only the large forms were found after death. In another the infection by peripheral cocci was noticed as early as August 7. From 10 to 20 per cent of infected corpuscles circulated in the blood until August 19, when some large pyriform bodies made their appearance. The blood contained both small and large parasites until August 25, when the animal was killed in a dying condition.

In the foregoing it has been tacitly assumed that these intraglobular coccus-like bodies are living organisms. This position without further proof would undoubtedly be open to objection, and hence the reason for considering them parasites will be discussed somewhat in detail. In the foregoing chapter all those changes which the red corpuscles undergo as the result of anaemic conditions have been described. Certain corpuscles when dried and stained presented numerous granules which varied more or less in size, the largest rarely exceeding  $0.5\mu$ . The coccus-like bodies resemble the larger granules very closely, and it might be argued that they are of the same origin. This is not so, however, for the following reasons: The coccus-like bodies appear *with or immediately before* the destruction of red corpuscles. The granules (or punctate cells) appear *after* the number has fallen below one-half the normal, and when the destruction ceases the punctate cells still persist or increase and the coccus-like bodies disappear. The coccus-like bodies are with rare exceptions in-

cluded in normal corpuscles; the granules belong to the large new cells (macrocytes). As to the bodies themselves, they are all of the same size in the same preparation of blood, while the granules vary considerably in this respect. Again, the granules are present in considerable numbers in the same corpuscle, while the coccus-like bodies are present singly or in a state of division; rarely two are found in the same cell.

When dried films are treated with one-half of one per cent acetic acid the coccus-like bodies come out distinctly as the cell fades. The granules can not be made to appear in this way. (p. 222.) Finally the punctate cells can be produced by artificial venesection, but the coccus-like bodies do not appear in the blood under this condition. The coccus-like bodies are thus of a character entirely different from that of the granules, although they take the same stain and appear together in the blood. (Plate IV, Fig. 3; Plate IX, Fig. 5.) Many of the same reasons will also apply in refuting the possible objection that they may be the result of disturbances of the blood other than those of a loss of corpuscles. Heinz\* found certain bodies stainable in methyl violet appear on the red corpuscles of rabbits twenty-four hours after the subcutaneous injection of phenyl-hydrazin and its derivatives. These bodies are described as "strongly refracting spheres which are attached, button-like, to the red corpuscle. Often they are connected with it by a pedicle, or they may be entirely free in the plasma surrounded by a shred of protoplasm." In Texas fever the corpuscles containing the coccus-like bodies are always of normal form and appearance. It would be difficult to find reasons for believing them to be the result of some chemical action on the blood corpuscles. The ticks, which might be regarded as secreting a poison in their parasitic life, are very scarce on the animals during the autumn and early winter, when the mild type of disease prevails. When they are most abundant, during the period of the acute disease, the coccus-like bodies give way to the pyriform bodies.

\* Arch. f. path. Anatomie, CXXII, S. 112.

If we admit their parasitic nature as highly probable we have still the question before us whether they are stages of the Texas fever parasite or of another parasite transmitted with it. This question can not be positively answered until, by methods akin to those of bacteriology, we shall be enabled to isolate the Texas fever organism and observe the transformation of one stage into the other, either in cultures or in the blood of inoculated animals. In the absence of such rigorous proof the presumption is nevertheless strongly in favor of the unity of this and the larger forms already described. We observe in the first place the appearance of both types of the disease in all outbreaks studied at the experiment station since 1889, though at different periods of the same season, the coccus-like bodies being associated chiefly with cool weather. An outbreak produced after the middle of September in 1889 developed cases containing the coccus-like bodies only. In one of these cases killed in a dying condition, the spleen and the liver were affected as in acute cases, but haemoglobinuria was absent. Several cases were observed in which there is a transformation of the mild into the acute type with a corresponding change in the form of the parasite.

Perhaps the strongest proof that the coccus-like bodies and the pyriform, amoeboid bodies are stages of the same parasite was furnished recently in an unexpected manner. Two cows inoculated with blood from healthy North Carolina cattle early in July, 1892, developed the acute type of Texas fever with the appearance of pyriform parasites within the red corpuscles. Both recovered, and the number of corpuscles was rising toward the normal, when, at the end of August, a relapse was detected in both animals. The number of corpuscles was rapidly falling again and many were infected with the coccus-like bodies. Reinfection from without can hardly be considered in these cases, as there were no ticks in the field and two control animals had normal blood throughout the season.\*

\* Since writing this four other cases, inoculated in the same manner, have passed through a relapse.

THE PROBABLE LIFE-HISTORY OF THE MICROÖRGANISM IN THE  
BODY OF CATTLE

We have thus far presented in a somewhat fragmentary manner the observations bearing upon this microörganism. It now remains to put them together in a way which will illustrate its probable development.

In the early stages of the high fever in a few acute cases, before the destruction of red corpuscles had gone far, very minute bodies were seen in fresh blood. Their form, so far as determinable (apochrom, 2 mm., ocular 8) appeared as an elongated figure of eight or ten short rods attached end to end. They had a very active Brownian motion in addition to a movement which carried them from one place to another in the field. This latter movement may have been due to currents in the liquid. They could not be detected in preparations stained with methylene blue. That this is the free form which precedes the parasitic stage must remain at present a mere conjecture.

*The (hypothetical) swarming or motile stage (intraglobular).—* We have already (on p. 213) referred to certain very minute, well-defined, bright, frequently motile bodies seen within the red corpuscles of healthy cattle at various seasons of the year. As might have been expected, these bodies were found in Texas-fever blood as well. It has also been stated that they vary more or less both in size and form. The question has frequently presented itself, whether some of these bright motile bodies were the progenitors of the coccus-like and the pyriform bodies of the Texas-fever parasite. Inasmuch as they are present both in health and in disease, only a most trying examination of the blood in many cases could decide whether certain forms only appeared in disease or not. These bodies are so minute and so inaccessible that it is by no means certain whether such a prolonged study would bear fruit. In the course of these investigations such a study was impossible, and we have simply to present the facts that these bodies are present in health and disease and that they vary in size and form. In one case it was difficult not to accept the hypothesis that some of the bodies are a stage of the microparasite. In the blood of this animal these bodies grew in

number with the peripheral coccus-like bodies and disappeared at about the same time. This view is presented simply to serve as a working hypothesis for such as are inclined to follow this phase of the subject more minutely. There is nothing in this hypothesis not in harmony with the positive observations concerning the Texas-fever microbe. Such a motile, swarming stage is one which can readily be conceived of as finding its way into the red corpuscle constantly in motion in the vessels of the body. Why it is not seen in every case may be explained by the same hypothesis which accounts for the presence of the peripheral coccus-like stage in the milder type of Texas fever. This hypothesis assumes a retardation in the intraglobular development of the micro-parasite by which the smaller stages remain long enough in the blood to be detected. If the retardation is still more pronounced, it is easy to conceive of the motile or swarming stage as circulating in the blood long enough to be detected.

*The stage of the peripheral coccus-like bodies.*—After the (hypothetical) swarm-spore has penetrated into the corpuscle it comes to rest, loses its bright, refrangent appearance, and attaches itself near the periphery of the corpuscle as a pale body which is only detected with difficulty in the unstained corpuscle. This body next undergoes division which is probably incomplete, for in the more advanced stages the two resulting bodies are as a rule still attached to each other. These remain close together while the infected corpuscle is circulating in the blood. This (p. 224) stage of the coccus-like body, like the preceding hypothetical stage, must be regarded as recognizable because of a retarded development of the microparasite. It is probable that this retardation of development in susceptible animals is due to meteorological conditions, such as low temperature of the air, and to partial immunity. In acute attacks the enormous multiplication of the parasite in the blood shows how rapid in such cases its development and how ephemeral these intermediate stages must be. The period of retardation may vary in length, but it seems probable that this stage may remain in the circulation at least several days.

*The stage of the larger forms (pyriform and spindle-shaped*

bodies)—The two coccus-like bodies resulting from division begin to grow and assume fusiform outlines. It is probable that they remain attached to each other at least for some time, for in stained preparations a very delicate stained line may occasionally be traced passing from one to the other. In this stage they stain very well in haematoxylin and basic aniline dyes. As they continue to enlarge, the two members of the pair remaining always of the same size, a more elongated, pear-shaped outline is assumed, and in the unstained condition a minute dark particle is observed in the broad end of each body. Under conditions not definable a larger or smaller number of the red corpuscles contain but one body. These unpaired forms are found most abundantly

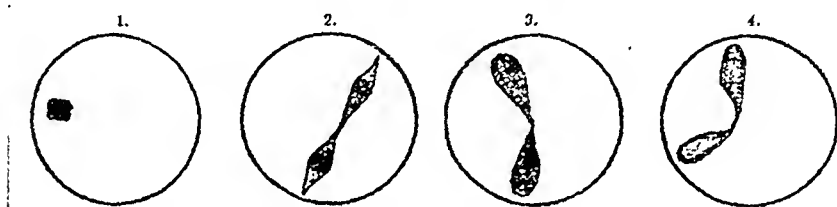


FIG. 3. INTRAGLOBULAR FORMS OF THE TEXAS-FEVER PARASITE

The shading shows the relative staining capacity with methylene blue. 1. The peripheral coccus-like body ( $0.6\mu$  long) in process of division (from the mild type). 2. Larger spindle-shaped forms from the capillary blood of the heart muscles. The free ends are but feebly stained. 3. Larger pyriform bodies from the same source staining entirely. 4. Pyriform bodies ( $2\mu$  long,  $1.5\mu$  wide at the widest portion) staining but feebly; from the circulating blood. (The last three forms from the acute type.)

dantly in the circulating blood, where they may manifest amoeboid changes.

The larger forms circulating in the blood do not stain so well as the somewhat smaller bodies found in the capillaries after death. This may be due to degenerative processes or to a transformation into some unknown reproductive state. The annexed figures illustrate, diagrammatically, the intraglobular stages of the Texas-fever parasite, i.e., those forms which have only been found in the blood during Texas fever, and very rarely in Southern cattle.

*Free bodies.*—These are set free after they have reached the preceding stage by the disintegration of the infected corpuscles.

They may be found in capillary blood of the heart muscle in abundance. Their most common location is in the kidneys, however.

No forms which might be interpreted as reproductive stages have been recognized at any time in the many cases which have been studied. That the organism multiplies very rapidly in the blood of susceptible cattle is demonstrated by the fact that the injection of a small quantity of infected blood gives rise to the disease. How does this multiplication take place? There are two possibilities in view. Either the large pyriform body, while within the corpuscle or after it is set free, may enter the reproductive stage and produce a generation of very minute bodies akin to the motile, bright intraglobular bodies seen in fresh blood, or there may be a free reproductive phase, distinct from the intraglobular forms, taking place in the blood.

#### THE NATURE OF THE TEXAS-FEVER MICROÖRGANISM AND ITS RELATION TO THE PARASITES OF THE RED CORPUSCLES OF OTHER ANIMALS AND OF MAN

It has been known since 1881 that the various types of malaria fever in man were accompanied by minute organisms living within the red corpuscles. This discovery by Laveran has been followed by confirmations in various parts of the world, and it is generally accepted that these intraglobular organisms are the cause of malaria. Stimulated by this important discovery, various observers have studied the blood of many animals (frog, turtle, and various birds), and have found therein certain minute parasites which likewise pass their life chiefly within red corpuscles. Much has been written upon the interrelation of these forms and their bearing on malaria in man. Nothing positive, however, has come of it, although there is a close resemblance between some of the parasites found in birds and those found in man. They all have in common the peculiar habit of living in the red corpuscles. Those of cold-blooded animals (frog and turtle) do not contain any pigment granules. On the other hand, those of birds and man do, as a rule, contain granules of dark pigment which is derived from that portion of the red cor-

puscle destroyed by them. The pigment granules are by some regarded as the more abundant the more retarded the growth of the parasite, and consequently the slower the destruction of the containing corpuscle. The parasites found in the blood of birds and man first appear as minute, slowly enlarging amoeboid bodies in the red corpuscles. Soon pigment granules appear. When of a certain size these bodies break up within the corpuscles into a variable number of spores. These are set free and begin life as a new generation by entering other red corpuscles and undergoing the same development. These cell parasites are not associated with a visibly diseased state of the animals in which they are found. In man it is well known that certain kinds of fevers known as malarial are produced by them.

The Texas-fever parasite differs in many important respects from all those thus far described. Its morphology is quite unique. It contains no pigment. It probably runs through its whole development in a short time, otherwise it would be difficult to account for the rapid destruction of red corpuscles. Nevertheless, no distinctly reproductive phase has been seen during four years of observation of a great variety of cases.

It is hardly within the scope of this report to go into any details concerning the parasites of the red corpuscles of other animals and of man. The literature of this subject has now grown quite voluminous, although the progress made is not very great, owing to the limitations of methods. None of these cell parasites have thus far been cultivated according to bacteriological methods, and it is not likely that they ever will be. Inoculations of blood containing them seem to succeed only when they are made on the same varieties of the same species of animals, according to Celli and Sanfelice,\* and even then success is limited to a small number of the cases inoculated. Observations are thus of necessity statistical and comparative rather than experimental, and must extend over a large number of cases before the significance of the various facts (p. 226) observed can be even formulated. Even then it is difficult to impart to others the conviction which comes from prolonged observation, while the

\* Fortschritte der Medicin, 1891. Nos. 12, 13, and 14.



desultory observations of many individuals lead to wide differences of opinion.

Classification of the parasites of red corpuscles has been attempted by Kruse and others and the various forms indicated under the following scheme:\*

Genus	Species	Variety
1. <i>Hoemogregarina</i> (Danilewsky).	<i>H. ranarum</i> , Danil <i>H. testudinis</i> , Danil <i>H. laertoe</i> , Danil	
	<i>H. columboe</i> , Grassi <i>H. danilewsky</i> , Kruse <i>H. aluci</i> , n. sp. <i>H. bubonis</i> , n. sp.	
2. <i>Hoemoproteus</i> (Kruse).....	<i>H. passeris</i> , Grassi <i>H. noctuoe</i> , n. sp. <i>H. alaudoe</i> , n. sp.	a.* c. a. c. a. b. c.
3. <i>Plasmodium</i> (Marchiafava et Celli).....	<i>Pl. malariae</i> , M. et C.	a. Quartanae. b. Tertianae. c. Quotidianae.

\* The letters refer to the relative rapidity with which the development goes on; *a* signifies slow; *b*, accelerated; *c*, rapid.

It seems improbable that the Texas-fever parasite will ever be ranged under any of these genera, and therefore a new genus has been created for it (*Pyrosoma*). The specific name (*bigeminum*) is derived from the peculiar character which this organism has of appearing in pairs within the red corpuscles. This name does not commit it to any special group of protozoan parasites, although it is not improbable that it may belong to the sporozoa to which most cell parasites belong. The peculiar pair of pyriform bodies within the red corpuscles might be homologized with the falciform bodies or crescents of the sporozoa, which in

\* Loc. cit., No. 14.

this case are without a cyst of their own and make use of the cell wall for this purpose.

The great rapidity with which this parasite multiplies in the system of susceptible cattle may perhaps be explained along lines suggested by R. Pfeiffer\* in his observations on *Coccidium oviforme* and *C. perforans* in the rabbit. These two species of sporozoa (the former inhabiting the bile ducts of the adult rabbit, the latter the intestinal epithelium of the young rabbits), Pfeiffer maintains, are one and the same, which runs through a rapid entogenic development, with the formation of an immense number of individuals in the intestines of young rabbits, and thereby causes a severe (mostly fatal) disease, while in the adult it remains largely restricted to the liver, where it runs through a slow partial development, and the spore produced requires conditions only found externally for its further development. Applying these observations to the Texas-fever organism, we may assume some dual development of the parasite, one taking place in susceptible, the other in insusceptible animals. Or the conditions may be much simpler in the latter, and depend largely on a simple repression of the multiplication of the parasite in the red corpuscles, owing to some unknown modifications of these bodies.

#### PROBABLE ACTION OF THE MICROÖRGANISM IN THE BODY OF SUSCEPTIBLE ANIMALS

This topic has been touched upon in the foregoing chapters, but only in a desultory manner, and the known facts are brought together here in a more compact form. The demonstration of the microörganism in the organs does not present any special difficulties. The organs were examined fresh or after being in the ice-chest for twenty-four hours, both in teased preparations and in sections. The teased preparations as well as the sections were examined in iodized serum to avoid any injury to the blood corpuscles. For the same reasons the sections were prepared with the razor and not on the freezing microtome. In such thin sections, or in teased preparations, some of the capillaries fre-

\* Beiträge zur Protozoen-Forschung. I. Heft.

quently remained intact, and the microorganisms could be made out as pale, roundish dots within the red corpuscle. Plate VII, Fig. 3, is drawn from an unstained teased preparation of the fresh spleen. Tissues were hardened both in strong alcohol and in Müller's fluid and alcohol, according to the usual procedure. The staining presented some difficulties, and in general the aniline dyes did not give satisfactory results. Haematoxylin in the form of Ehrlich's acid haematoxylin has proved very satisfactory in bringing out the intraglobular parasites. In tissues hardened in Müller's fluid the outer layers showed a peculiar modification of the parasites. Instead of appearing as blue bodies, they assumed a brownish-red color. This was especially noticeable in tissues which are very delicate, such as the choroid plexus. In these all the parasites appeared brownish-red instead of blue. This may be due to the action of the Müller's fluid. Tissue hardened in alcohol, while it demonstrates the intraglobular bodies very distinctly, does not preserve the corpuscles so well.

The destruction of red corpuscles by the microparasite within them is the main fact in the pathology of Texas fever. There are, however, some secondary phenomena associated with this destruction, which account, in part at least, for the peculiar lesions of this disease. The infected corpuscle remains in the circulation as long as the contained parasite is below a certain size. Thus, in the mild autumnal form of the disease the number of circulating corpuscles invaded by the coccus-like bodies is rarely below 5 per cent, commonly from 10 to 30 per cent, and at times near 50 per cent. The corpuscles are not changed in form or size, and in fact the parasites are very small when compared with the size of the corpuscle, and only brought out distinctly by staining. When the parasite has reached a certain size we may assume that the corpuscles lose their flexibility and adaptability to the minute channels or capillaries and become lodged in them, forming emboli, so to speak. The capillary becomes obstructed, and red corpuscles are wedged in behind the infected ones. It is highly probable that at this time a favorable opportunity is offered to the free, earliest stage of the micro-

organism to attack the remaining corpuscles, otherwise it would be difficult to understand why capillaries are frequently found which contain, to all appearances, only infected corpuscles. It may be that other factors come into play, such as the changed specific gravity of the infected corpuscles, by which their relation to the blood plasma becomes changed and in virtue of which they act as foreign bodies in the vessels. Whatever may be the reason, the fact remains that the paucity of infected corpuscles in the blood taken from the large vessels and the heart is counterbalanced by a very extensive infection of the corpuscles found in the capillaries. The smaller the capillary the higher the percentage (p. 228) of infected corpuscles. In the white substance of the brain, the capillaries in a section were sometimes found completely filled with red corpuscles and every corpuscle was infected. Similarly, capillaries have been observed both in sections of hardened tissue and in teased preparations of fresh tissue from the spleen, kidneys, intestinal mucosa, omentum, plexuses of the brain, heart muscle, and red marrow of the ribs, which were either completely or partly filled with infected corpuscles alone.

This capillary plugging or embolism may account, to some extent at least, for the enormous distention of the spleen and for the degenerative changes of the parenchyma of the liver. The perinephritic sanguinolent oedema so frequently observed on post-mortem examination is probably due to the complete filling up of the vascular system of the kidneys with infected and uninfected corpuscles. Similarly the ecchymoses in the calyces of the pelvis may be accounted for by this condition.

Another phenomenon of interest is the remarkable injection of all pathological growths of a vascular character, such as old fibrous adhesions and pleuritic fringes. Similarly vascular fringes found on the omentum covering the paunch, and on the origin of the large vessels at the base of the heart, appear as dark red spots. Here microscopic examination shows the same abundant infection. The intense injection of the vascular plexuses of the brain cavities is associated with extensive infection within the capillary network. This injection of the entire capillary system of the body may be largely aided by the presumable rise of blood

pressure which must take place after the enlargement of the liver and the engorgement of the spleen and kidneys practically shut these organs out of the general circulation.

While the skeletal muscles show but slight infection, the heart muscle is severely involved. Probably owing to the smaller caliber of its capillaries and the constant contraction of the muscular walls, a favorable opportunity for the lodgment of infected corpuscles is afforded. In the capillaries of the heart muscle the infection of corpuscles is always very great, and freed forms of the parasite are abundant. The capillary plugging will account for the almost constant ecchymoses of the external and internal surfaces of the ventricular walls.

The breaking up of the infected corpuscles probably takes place in the capillaries over the entire body, for, as stated above, freed parasites are found in the capillaries of the myocardium after a certain period of fever. This leads to the presence of freed haemoglobin in the blood (haemoglobinaemia). This condition was strikingly demonstrated in the case of a fetus about three months old taken from a cow which had succumbed in the acute stage. The amniotic fluid has a beautiful wine-red color. It is probable that many infected corpuscles, which break away from the capillary plugs are carried into the kidneys, where the final dissolution takes place. Otherwise it would be difficult to account for the usually enormous numbers of free as well as intraglobular parasites which are found in the kidneys toward the end of the fever.

The haemoglobinuria observed in nearly all acute cases may be due in part to a transudation of the haemoglobin dissolved in the blood, in part to the destruction of red corpuscles in the kidney itself. The same may perhaps be true of the material transformed into bile by the liver. This organ is, as a rule, heavily infected, though not to the extent observed in the kidneys. The bile contains to all appearances a very large quantity of bile pigment. This may be derived in part from the (p. 229) dissolved haemoglobin in the general circulation and in part from the corpuscles undergoing destruction in the capillaries of the liver itself.

The cause of the high temperature in the later stages of the fever, when the pathological changes are well under way and the blood is loaded with the debris of corpuscles and free parasites, may not be open to discussion. In the earliest stages, however, the explanation of waste products in the blood does not seem to follow in every case. In a few the fever was high, although there was no apparent reduction of red corpuscles. It must be stated that in view of the fluctuations to which the number of corpuscles is subject the counts in these cases may be somewhat misleading. Yet on the whole the initial fever seems to be caused by something other than the destruction of the red corpuscles, and we may invoke two possible causes, leaving their determination to more accurate continued observations on single cases. These are the multiplication of the parasite in the blood, perhaps independent of the corpuscles and the thrombosis of capillaries in the nerve centers.

The question of a cyclical destruction of red corpuscles corresponding to the different generations of parasites is an interesting one, but the observations put on record in the appendix do not give us any definite information. In acute cases after the first few days the fever is continuous, or nearly so, and does not indicate any intermission or remission of the acting cause. Whether the individual generations follow one another so rapidly, or whether there are a number of generations intermingled, has not been determined. To the eye there is more or less uniformity in the size of the parasites observed in any given case throughout the body. They may be all minute in the stage of the coccus-like bodies, or they may all be unusually large, or they may all be in a stage intermediate between these extremes. It should be stated, however, that in a few cases the fluctuation in the destruction of the red corpuscles was regular enough to suggest a period of from one and a half to two weeks in such cases.

What becomes of the microparasites in those cases which recover? We have already signalized the setting free of the parasites and their accumulation in large numbers in the kidneys. Further than this the observations do not go. The parasites are perhaps destroyed by a combination of circumstances, one

of which is the small number of red corpuscles finally left for infection. Thus in blood containing only one and a half to two million red corpuscles fully one-half are enlarged, embryonic forms which may not be so well fitted for the growth of the parasite. Another circumstance may be the unfit condition of the blood due to the presence of the very débris which the parasites have aided in producing.

OUTBREAK IN WHICH THE TEXAS-FEVER PARASITE HAS BEEN  
DEMONSTRATED

The parasite of Texas fever, or more particularly the coccus-like and the larger pyriform stage of this microörganism, have been demonstrated in the following outbreaks:

- (1) In the spleen of a case from an outbreak in Virginia, September, 1886.
- (2) In the organs of cases from an outbreak in Maryland, September, 1888.
- (3) In the blood and the organs of cases from an outbreak on the experiment station (North Carolina infection), August to October, 1889.
- (4) In the blood and the organs of cases from an outbreak on the experiment station (North Carolina infection), September to November, 1889.
- (5) In the blood and the organs of cases from an outbreak on the experiment station (North Carolina infection), August to November, 1890.
- (6) In the blood and the organs of cases from an outbreak on the experiment station (Texas infection), August to October, 1890.
- (7) In the spleen of a case which died in North Carolina, June 29, 1891.
- (8) In the blood and the organs of cases from an outbreak on the experiment station (North Carolina infection), August to November, 1891.
- (9) In the blood of a case from an outbreak in Pennsylvania, November, 1891. (Specimens of organs and urine sent by George Jobson, Jr., v.s.)

- (10) In the organs of a case at Fort Smith, Ark., March, 1892. (Preparations sent by R. R. Dinwiddie, v.s.)
- (11) In the organs of a case produced by the intravenous inoculation of blood from North Carolina cattle, July, 1892.
- (12) In the organs of cases from an outbreak produced at the experiment station in the usual way by North Carolina cattle, August and September, 1892.
- (13) In the organs of cases from an outbreak in New Jersey, August, 1892.
- (14) In the spleen and blood of cases from an outbreak at Camden, N. J., August, 1892. (Specimens sent by Drs. Miller and Seilers.)

In Nos. 7 and 13 there were the usual lesions (haemoglobinuria, etc.), observed by Dr. F. L. Kilborne at the autopsies. In No. 9 there were the usual fatty degeneration and bile injection of the liver and haemoglobinuria. The diagnosis of Texas fever was thus assured in all the outbreaks mentioned.

#### THE PRODUCTION OF TEXAS FEVER IN CATTLE BY THE INOCULATION OF BLOOD FROM CASES OF THIS DISEASE

The demonstration that Texas fever is caused by a certain microörganism is not absolutely made by showing that it is always associated with this disease and not observed in health. It may be argued, that such bodies are the concomitant rather than the cause of the fever. Nevertheless it may be said that no microörganism constantly associated with a given infectious disease has yet been found which is not demonstrably or presumptively the cause of the disease. Hence the probability that the microparasite described is the cause of Texas fever is very high, although the demonstration can not be made until such organism can be cultivated in some manner outside of the animal body and inoculations made with pure cultures. There is nothing today to encourage us in the hope that parasites so highly adapted as the one under consideration will ever submit to the crude culture methods successful with many bacteria.

The high probability that we have the cause of Texas fever before us is increased by the fact that when blood from cases of



this disease is injected into the circulation of healthy susceptible cattle, the disease is produced and the microparasite appears in the blood under the same conditions under which it becomes manifest in the natural disease. There is still the possibility before us that the microparasite is transmitted in the diseased blood and that some unknown agent has been transmitted with it which is the true cause of the infection. It is useless to discuss this further, and each reader must form his own opinion of the value of the experimental evidence adduced in this report.

Before quoting our experiments in the production of the disease, a few observations on the attempt of others to produce it are in order.

Dr. D. E. Salmon in 1880 (4, p. 303), made a number of inoculations with tissues and fluids taken from cases of Texas fever, some of which were successful:

(1) November 7, 1879. Calf 6 to 8 months old inoculated subcutaneously with bile and blood kept ten days in a sealed pipette. No result.

(2) September 14, 1881. Yearling inoculated subcutaneously with 5 cm<sup>3</sup> blood from a case dead three or four hours. No result.

(3) September 29. Yearling bull inoculated subcutaneously with 5 cm<sup>3</sup> blood containing some spleen pulp, which had been kept twenty-two hours in sealed pipette.

(p. 231)

(4) Red cow inoculated as No. 3; also drenched with a mixture of blood, urine, and bile.

(5) Heifer received a subcutaneous injection of 5 cm<sup>3</sup> of bile.

(6) Bull 3 years old drenched with one ounce of urine.

(7) Steer 2 years old drenched with one ounce of bile.

(8) Cow received 5 cm<sup>3</sup> of urine under the skin.

Of the cases from Nos. 3 to 6, inclusive, No. 3 and No. 4 reacted with a high temperature and No. 4 became very weak and emaciated. In 1883 (5, p. 34) three additional experiments are reported. A steer and a heifer, 2½ years old, received August 7 subcutaneous injections of spleen pulp suspended in water. The spleen pulp had been kept in a sealed tube for seven days. Neither animal became affected. A third animal, a cow which

has been inoculated subcutaneously with fresh splenic pulp, October 3, was taken sick in ten days and died three days thereafter. There were evidences of haemoglobinuria. Two young animals drenched with the same splenic pulp did not become seriously affected.

A number of additional inoculations were made with cultures of a micrococcus cultivated from the spleen of a case of Texas fever with negative results in all cases.

Dr. Billings gives the notes of a case inoculated with cultures of what he regards as the Texas fever bacterium (8, p. 100). We have already commented on this case. In this connection it is sufficient to say that the proof of Texas fever has not been brought in this case, although it should have been above reproach, since it is supposed to establish the etiology of Texas fever. The observations in this report show that there is no Texas fever without a marked reduction in the number of red corpuscles. This is the essential sign of Texas fever. Secondary to this are lesions of liver, spleen, and kidneys, and haemoglobinuria and the presence of embryonic corpuscles in the blood. There is nothing in the autopsy notes as published by Billings to demonstrate the presence of Texas fever in the absence of red water. It is also curious that in his experiment the young animal of 5 months should take the disease more severely than the "large red cow," since calves are proverbially resistant.

In the report of Paul Paquin (9, p. 46) we find the following statements:

Texas fever is transmissible not only from Southern stock to susceptible Northern cattle, but under favorable circumstances is inoculable between Northern natives, although in the ordinary course of things in our climate transmission does not occur. We have inoculated native Missouri cattle with spleen and liver pulp from other diseased natives and produced typical cases of Texas fever, but it took large doses of virus. The rapidity of the course of the malady depends much on the origin and age of the virus. It was more rapid from old pulp kept in warmth and properly preserved than it was from virus of fresh matter, and it seems impossible to cause severe Texas fever with fresh urine, whilst the same exposed to warmth awhile becomes dangerous.

There are no experiments reported to convince the reader of the truth of these statements, though the direct transmission of disease from Southern cattle and sick natives to susceptible cattle by inoculation has been confirmed by us. Why old spleen pulp and old urine should be more dangerous, excepting as producers of septic conditions, is by no means clear. We should believe the contrary. We have no information at all as to how the inoculation was made, or any to show that the inoculated animals did contract Texas fever, excepting the bare statement that the inoculations were successful.

R. R. Dinwiddie (10) made subcutaneous inoculations upon four different animals with fluids and tissues from cases of Texas fever. We are (p. 232) glad to see the experiments reported, so that they may be estimated at their true value. The inoculations were made with fresh urine, spleen pulp kept over night, with bile kept in a sealed pipette, and with a culture of a micrococcus from the liver of a case of Texas fever. These inoculations proved negative. A fifth animal which received spleen pulp kept over night as a drench remained well. We have no reason to doubt the accuracy of these results. The negative outcome may have been due to the fact that only young animals were used, and that the season was perhaps too far advanced for experimental cases to succeed.

In all of these experiments the uncertainty of the conclusions reached as regards the negative results must be evident to all who have read the foregoing part of this report. Many of the cases which to all appearances were not affected may have passed through a mild attack, recognizable only by the microscopic examination of the blood corpuscles and a determination of their number.

Our own experiments were made mainly with fresh material, and this was injected under all the skin and into the blood directly. Nine inoculations were made in all.\* We shall in this place only refer to the important points in each of the following special cases:

\* Five additional cases of Texas fever were produced with the blood of healthy North Carolina cattle (page 264).

(1) On September 1, 1890, No. 111, a heifer about 21 months old, received into one of the jugular veins 13 cc. of whipped blood. This was obtained from No. 128, which had just died, and in whose blood there was a large number of infected corpuscles. The defibrinated blood was kept in a warm chamber at  $35^{\circ}\text{C}$ . for three hours before the injection. An examination of the table compiled shows a decided fall in the number of red corpuscles on the thirteenth day, and several days thereafter a considerable number of new red corpuscles (macrocytes) were found in the blood. There can be no doubt that this was a mild case of Texas fever. The subsequent gradual weakening of this animal and death three months after the inoculation could not be accounted for.

(2) On September 16, 1890, a similar injection with defibrinated blood was made on No. 142. The blood was taken from the heart of No. 90 about one-half hour after death, and after defibrinating, it was kept at  $35^{\circ}$ – $40^{\circ}\text{C}$ . for one and one-half hours before it was injected. In the table was observed a marked fall in the number of red corpuscles at three different times from two to three weeks apart. The animal fully recovered subsequently. Neither of these cases would probably be considered conclusive evidence that the disease can be reproduced in this way. The seven following cases will dispel any doubt on this point.

(3) On September 19, 1891, a portion of the heart muscle of No. 181, just dead, was pounded in a mortar with sterile normal salt solution. The resulting reddish fluid was filtered and injected into the jugular vein of No. 182, after standing in a warm chamber for about one hour. The table compiled in this case leaves no doubt as to the nature of the disease. The temperature rose on the sixth day in the evening, and a high evening temperature was observed for ten days thereafter. A high morning temperature was first noted on the eighth day, and the fever remained continuously high for at least four days thereafter. The number of blood corpuscles had fallen from 6,000,000 to 2,000,000 eleven days after the inoculation. The Texas-fever parasites were found in the blood. The animal fully recovered subsequently.

(p. 233) (4) On the same day blood was withdrawn from the jugular vein of No. 181, then still alive, and injected at once into the jugular of No. 185. The whole operation lasted one or two minutes. Of this blood, which contained at the time perhaps one-half to one per cent infected corpuscles, two syringefuls, or 28 cc., were injected. The disease produced in this animal was severe enough to leave no doubt as to its nature. The evening temperature was high on the third day and was low again on the ninth day. The continuous high temperature lasted four days. The number of blood corpuscles had fallen from 5,000,000 to 2,000,000 on the tenth day. The Texas-fever parasites were found in the blood. The animal fully recovered subsequently.

(5) No. 186 was treated precisely as No. 185, at the same time. A very severe case of Texas fever was the result. The temperature and the loss of red blood corpuscles were the same as in No. 185 (see page 182 for curve). On the ninth day she could scarcely stand, and was trembling and quivering over the whole body. A syringe of blood was withdrawn at the time from a jugular vein for other inoculations, and the operation was followed at once by convulsions and death. The very advanced lesions of the liver and spleen, the dark red, port-wine-colored urine, and the immense number of infected corpuscles in the various organs, made this case one of the most severe of the season.

In 1892 four cows were inoculated with blood obtained from a case of the disease. All became affected within a week and three died. The more important facts in connection with these inoculations are reproduced here.

On August 27, blood was withdrawn from the left jugular vein of No. 222, then suffering with the disease. In the blood a small number of large intraglobular parasites were found. The skin over the jugular was shaved and washed with 0.1 per cent mercuric chloride and the vein opened with a scalpel. The blood was caught in sterilized bottles, containing glass beads, and defibrinated by shaking vigorously for ten minutes. The bottles were kept in a water bath at 40°-42°C. The injections were

performed not longer than fifteen to twenty minutes after the withdrawal of the blood from No. 222.

(6) No. 197, a cow 6 years old, received into the left jugular 14 cc. (one syringeful) of this blood.

(7) No. 277, a cow 11 years old, received under the skin of the neck  $\frac{1}{2}$  cc. of the same blood in four different places, i.e., 2 cc. in all.

(8) No. 228, a cow 7 years old, received subcutaneously  $\frac{1}{2}$  cc. in two places, i.e., 1 cc. in all.

No. 197 died quite unexpectedly September 4, eight days after the inoculation. The temperature had been high since August 31. The autopsy left no doubt as to the nature of the disease.

No. 227 died September 9, thirteen days after the inoculation. The temperature had risen and other symptoms of disease had appeared September 2. On the day of death the red corpuscles had fallen to 1,500,000. The autopsy revealed the usual lesions of Texas fever in a very marked degree. The urine was visibly free from haemoglobin. The small number of red corpuscles just before death indicated that the period of haemoglobinuria was past.

No. 228, which had received the smallest dose, reacted as promptly as the foregoing, with a high temperature. The usual symptoms appeared, but more tardily, and the animal finally recovered. On September 14, the red corpuscles numbered 1,500,000. From this time there was slow improvement in the condition of the blood.

(9) One bottle of the defibrinated blood with which the preceding (p. 234) animals had been inoculated was placed in a refrigerator at an average temperature of 50°F. (10°C.) from August 27 until August 30. On this day 14 cc. (one syringeful) was injected into the left jugular vein of No. 200, a cow 8 years old. After five days of elevated evening temperature and two of continuous high temperature, this animal succumbed September 8. The organs presented the usual lesions of Texas-fever. The urine had a dark port-wine color. In the various organs and the blood many infected corpuscles were detected.

With these positive results before us we need not hesitate to make the statement that there is something in the blood of the cattle during Texas fever which, introduced into the body of healthy susceptible cattle, gives rise to the disease. This something is capable of reproducing itself indefinitely in the blood of susceptible animals. In all cases there had been multiplication of the Texas-fever parasite, and these inoculations furnish additional proof that this parasite may be regarded as the cause. These inoculations show, also, that a comparatively small quantity of blood from diseased cattle placed under the skin is capable of causing a severe and even fatal infection. In this respect the microörganism seems to have as powerful an effect as the bacteria which produce acute fatal forms of septicaemia, and seems to be capable of almost equally rapid multiplication. The sojourn of three days in a refrigerator did not destroy the vitality of the microörganism as it exists in the blood. The very severe inoculation disease produced in 1891 and 1892, as compared with 1890, is partly to be accounted for by the fact that only old animals were used latterly, while in 1890 the animals were young. The observations made in the field experiments and by former observers that the susceptibility seems to increase with age, provided there has been no exposure to the disease at any time in life before, is thus indirectly confirmed by inoculation. The very striking susceptibility of cattle to this disease was furthermore demonstrated by the intravenous inoculation of three guinea-pigs at the same time with three of the cases cited above (Nos. 6-8, inclusive). These animals remained perfectly well, though they had received relatively to their body weight a very much larger quantity of the defibrinated blood.

#### THE INOCULATION OF ANIMALS OTHER THAN CATTLE WITH TEXAS-FEVER BLOOD

The inoculation of animals other than cattle had a twofold purpose: first, to determine whether other domesticated animals are likely to become infected with the microparasite and perhaps cause the dissemination of Texas fever, and, second, to find some small animal to take the place of the much more costly cattle in

the study of the parasite and the disease. This was especially desirable, since this parasite can not be cultivated outside of the animal body.

*Sheep*.—Since sheep and cattle are so closely related it was thought that the disease might perhaps be induced in them. For this purpose a lamb was used. A syringe of (7 cc.) of blood was drawn from the right jugular of cow No. 184, which was very sick at the time, and whose blood contained the microparasite in small numbers, and injected at once into the left jugular vein of the lamb. The operation was performed October 1, 1891; the blood contained 10,442,000 red corpuscles in a cubic millimeter. No parasites of any kind were detected in them.

(p. 235)

October 13—Red corpuscles 8,282,000. Nothing abnormal detected.

October 27—Red corpuscles 11,538,000. Several bright intra-lobular bodies seen in the fresh preparation, but no parasites.

From October 1 to October 27 the temperature was taken twice daily. It fluctuated between 101 and 103.

Though the inoculation was made somewhat late in the season the outcome plainly indicates no susceptibility of sheep to this disease.

*Rabbits*.—September 20, 1889, immediately after cow No. 54 had been killed, a quantity of spleen pulp containing many corpuscles infected with large paired parasites was mixed with sterile salt solution. The reddish liquid was injected into the ear vein of three rabbits. No rise of temperature and no symptoms of disease was noticed. One rabbit was killed on the seventh day and the blood and organs carefully examined for infected corpuscles with negative result. The others were watched for several months, but nothing abnormal detected in their action. The second rabbit, which had become scabby, was killed January 18, 1892. The various organs and the blood were examined microscopically with negative result. The following may also be cited:



October 1, 1891—With the blood of cow No. 184 two rabbits (Nos. 140, 141) were inoculated at the same time with the lamb. Each received 1 cubic centimeter into the ear vein.

No. 140 (black rabbit) showed no external symptoms of disease. The blood was examined twice and no infected corpuscles found.

October 19, 1891—6,537,000 red corpuscles in a cubic millimeter.

December 3, 1891—7,134,613 red corpuscles in a cubic millimeter.

No. 141 (white rabbit) remained equally well. The following blood examinations were made:

October 19, 1891—5,268,000 red corpuscles in a cubic millimeter.

December 3, 1891—4,533,000 red corpuscles in a cubic millimeter. Infected corpuscles absent.

*Pigeons.*—September 28, 1891. Blood containing infected corpuscles is drawn from the jugular vein of cow No. 186 and injected at once into the wing vein of three pigeons (Nos. 2, 3, and 4). In a fourth pigeon (No. 1) the blood failed to enter the vein and was deposited in the surrounding connective tissue. Each received about 1 cc.

No. 1 died October 13, though not from the inoculation, as its feathers were ruffled at the time of the operation and it was probably not well at that time. Examination of the blood and organs negative. The other pigeons remained well. On October 5 the blood of No. 3 contained 3,926,800, that of No. 4, 4,094,300 red corpuscles, in a cubic millimeter. They were killed January 22, 1892. The blood of No. 3 was searched in vain for parasites.

*Guinea-pigs.*—August 27, 1892. Blood was drawn from the left jugular of cow No. 222, affected with Texas fever, into sterile wide mouthed bottles containing glass beads and defibrinated by shaking vigorously. Three guinea-pigs were inoculated: No. 1 received into the exposed jugular 1 cc. of defibrinated blood; No. 2 received into an ear vein  $\frac{1}{2}$  cc.; No. 3 received into an ear vein 1 cc.

The injections were completed fifty to seventy minutes after the blood had been drawn from No. 222. The injection into the ear vein was a perfect success in the two cases on which it was tried. These guinea-pigs remained entirely well. The blood was examined from time to time both in fresh and in dried and stained

preparations, but the corpuscles were not counted, owing to the pressure of other work. There was no evidence, however, from the microscopic examination, of any change from the normal condition or of any infection. The guinea-pigs were watched for more than a month after the inoculation.

Strongly contrasting with the result of guinea-pigs is that obtained (p. 236) with the same blood on cows. The largest quantity injected into the circulation of the guinea-pigs was relatively to the body weight not less than twenty-five times greater than the largest dose, and three hundred times greater than the smallest dose injected into the cattle. Yet all four cows contracted Texas fever and three died.

Of other observers who have tried to produce Texas fever in other animals we find Paquin (9, p. 46) making the following statement: "We have succeeded also, though with great difficulty to induce the disease in sheep, guinea-pigs, white mice, white rats, and very rarely rabbits, kittens, and swine. The germs may be reproduced by inoculation of liver and spleen pulp in any of these subjects, but the quantity must be large and the gross typical spleen lesions are not always to be found." Inasmuch as spleen lesions are associated with a variety of infectious and septic diseases in animals, and as there is no record of other lesions peculiar to Texas fever in these inoculated animals, we are compelled to call in question the accuracy of the diagnosis in these cases.

The inoculations made by us demonstrate that sheep, pigeons, rabbits and guinea-pigs are to all appearances insusceptible to this disease, whereas in cattle the disease may be invariably produced by the injection of infected blood. It is to be hoped that opportunity will be presented the coming summer to try other species of animals.

#### THE TRANSMISSION OF TEXAS FEVER BY MEANS OF THE CATTLE TICK

##### *Boöphilus bovis* (Riley) Curtice

It has been a more or less prevalent theory of cattle-owners in the districts occasionally invaded by Texas fever from the

South that ticks are the cause of the disease. Mr. J. R. Dodge, (2) in his historical report of this plague, mentions the fact that in 1869 an outbreak in Chester County, Pa., was believed to be caused by ticks. Gamgee in 1868 (2) states: "The tick theory has acquired quite a renown during the past summer, but a little thought should have satisfied anyone of the absurdity of the idea." The officers of the Metropolitan Board (1, p. 1084) and most subsequent observers seem to have entertained the same view of the harmlessness of the cattle tick as a carrier of the infection. In fact, few observers have given it any thought. In the entire report of F. S. Billings we find no reference whatever to these pests. Paquin (9, p. 45) states that he has "found the parasites also in *ticks bloated with blood of infectious Southern cattle*. So this must be added to the list of sources." But the ubiquity of this "germ" rather predisposes one against any belief in its existence if we did not have sufficient positive evidence that bacteria have nothing to do with the disease. The statement thus depends simply upon the finding of a "germ" in adult ticks resembling that found in diseased cattle, and in fact everywhere else (waters, soil, manures from the South, urine, bile, liver, spleen, kidneys, etc., of infectious Northern stock). Experiments to demonstrate the relation which ticks bear to Texas fever were not made.

Nothing positive was thus contributed to the elucidation of the action of ticks in carrying the disease until the subject was taken up at the Experiment Station of the Bureau near Washington, in 1889. Here it was found by experiments to be detailed in the remainder of this report that the disease can be produced by ticks hatched artificially in (p. 237) the laboratory, without the presence of Southern cattle. Before giving in detail the experiments which led up to the final determination of this important discovery a few facts concerning the cattle tick which have come under our observation are necessary for the information of the general reader. We do not propose to give anything more than a general account of the tick, leaving problems of biology and morphology to those pursuing special lines of work in this field.

THE CATTLE TICK (*BOÖPHILUS BOVIS*)

(Plate X.)

The first description of this parasite was made by Prof. C. V. Riley, in 1868, under the name *Ixodes bovis* (2, p. 118):

*Ixodes bovis* Riley.—A reddish, coriaceous flattened species with the body oblong-oval, contracted just behind the middle, and with two longitudinal impressions above this contraction, and three below it more especially visible in the dried specimen. Head short and broad, not spined behind, with two deep, round pits. Palpi and beak together unusually short, the palpi being slender. Labium short and broad, densely spined, beneath. Mandibles smooth above with terminal hooks. Thoracic shield distinct, one-third longer than wide, smooth and polished; convex, with the lyrate medial convexity very distinct. Legs long and slender, pale testaceous red; coxae not spined. Length of body 0.15 of an inch; width 0.09 of an inch.\*

The generally accepted idea as to the harmlessness of this parasite caused it to be neglected as an object of study until 1889, when our preliminary experiments seemed to indicate that ticks must be present to convey the infection from Southern to Northern stock. Hence, Dr. Cooper Curtice, at that time in charge of the investigation of animal parasites, began the study of the life history of this species.† It was discovered quite accidentally that adult females kept confined in bottles or other glass receptacles always lay their eggs. Such a stock of eggs furnished the starting point of Dr. Curtice's investigations. The eggs were placed in covered glass dishes containing a little soil and kept in a warm place. After a period of three to four weeks the young ticks appeared. These were placed on a calf kept in an artificially heated stable, as the season was already advanced (November 15). The earliest or larval stage as it emerged from

\* We simply quote this description here as a matter of historical interest, without comment as to its accuracy. We may state, however, that the color of adult females is not reddish. The back is olive brown, the belly slate colored. The dimensions given in this diagnosis probably belong to an adult male. For the dimensions of the parasite in its different stages, see this chapter.

† The biology of the cattle tick. Journ. of Comp. Medicine and Veterinary Archives. July, 1891, and January, 1892.

the ovum had three pairs of legs. After one week's sojourn on the calf it was ready to moult. The emerging nymphal stage was provided with an additional pair of legs. After another week's life on the calf the tick was ready to moult a second time and become sexually mature. Curtice thus showed that in this particular species there are two periods of moulting before the parasite becomes matured. He likewise created for it a new genus (*Boöphilus*). Dr. George Marx has given more or less attention to the classification of ticks, and places the species under consideration as follows:\* Class, *Arachnida*; order, *Acari*; suborder, *Cynorhoesta*; family, *Rhipistomidae*; genus, *Boöphilus*; species, *bovis*.

In our experiments with this cattle tick we have confirmed and extended the observations recorded above chiefly in the direction of the life history, since this is the most important aspect in its relation to Texas fever.

(p. 238) The laying of the eggs may be observed by anyone by simply placing full-grown ticks in some vessel from which they can not escape. The tick remains quiet for from two to four and one-half days, according to our observations; then a few eggs will be observed on the mouth parts, which gradually increase in number. The period of oviposition varies somewhat. Confined in bottles, for instance, at a temperature of 68°-78°F. the laying was observed to continue from eight to fifteen days in a lot of 23 mature ticks, each one of which was kept in a separate bottle. The number of eggs varies in general with the length of the egg-laying period. Those which took the longest time laid the largest number. Of 4 ticks laying from twelve to sixteen days, each averaged 118 mgr. ( $1 \frac{13}{16}$  grains) of eggs. Careful counting gave an average of 1,300 eggs per grain. If we take the actual weight of all the eggs laid by the 23 ticks, which is 2.41 grams ( $37 \frac{1}{8}$  grains), a single full-grown tick averages about 2,100 eggs. Ticks do not need to be fully gorged with blood before they are capable of laying eggs. Even such as are half-grown will begin to lay after a few days, but the number is much less than that laid by the large, gorged individuals. Tests showed that 40 half-grown

\* Proc. Entomological Society of Washington, ii, p. 232.

ticks laid no more eggs than would have been laid by 7 or 8 full-grown individuals. During the process of oviposition the female slowly shrinks in size, and when it is completed she appears shriveled and not more than one-half or one-third her former size. The eggs appear as dark, brownish-red masses of oval bodies. The color varies somewhat, and its depth appears to be connected somehow with the quantity of blood with which the female is gorged before oviposition. Measurements of freshly laid ova in 1889 made the long diameter 0.519 mm., the transverse 0.38 mm. Measurements in 1892 gave nearly the same figures, 0.496 and 0.384 mm. They are thus, roughly speaking, one-fiftieth of an inch long and one sixty-sixth of an inch broad at their widest portion.

When masses of ova are placed in glass dishes with a little soil or some leaves and a few drops of water, and the dishes kept closed with glass covers so that the emerging young may not escape, the incubation goes on without any difficulty. The period required for the young to emerge from the shell varies very markedly with the surrounding temperature. In Curtice's first experiment it required from three to four weeks. The temperature of the bacteriological culture room where they were kept could not have been lower than 70° to 80°F. at that time. This relation to temperature is well exemplified in the following experiments:

(1) Ticks sent from North Carolina and received here July 29, 1890, have laid a considerable number of eggs on the way. These are placed in glass dishes and kept in the laboratory. Many young ticks moving about on August 13. Here the period of incubation was from fifteen to eighteen days. The weather during this time was very hot.

(2) Eggs two to three days old placed in glass dishes August 8. Young ticks appeared August 29. Period about twenty-four days.

(3) Eggs several days old placed in dishes August 13, 1890. Young ticks appear in large numbers September 4 and 5. Period approximately twenty-five days.

(4) On September 17, 1890, eggs two to three days old placed in glass dishes. Young ticks first appear October 23, and their number increases until October 28. Period about forty days.

(5) Eggs one to three days old are placed in glass dishes September 20, 1890. Young ticks present in abundance November 1. Period about forty-three days.

(6) Eggs one to three days old are placed in glass dishes September 23, 1890. Young ticks begin to appear November 1. Period about forty days. The eggs from experiments 4, 5, and 6, were taken successively from the same adult ticks. The temperature of the laboratory at this time was  $75^{\circ}$ – $80^{\circ}$ F. during the day, but fell  $5^{\circ}$  or  $10^{\circ}$  at night.

(p. 239) (7) Eggs one to two days old placed in dishes October 6 and 9, respectively. The dishes were kept on shelves several feet above a steam heater. On November 9, all eggs were found hatched out. Period about thirty days or less.

(8) Eggs two to four days old placed in dishes October 9, 1890. Over steam register only a part of the time. A few young ticks appeared November 15. Hatching completed November 17. Period about thirty-eight to forty days.

From these recorded dates it will be seen how essential a high temperature is for the rapid development of the embryo in the egg. The period of development may vary from fifteen days to six or seven weeks, and may perhaps be prolonged still more by lower temperature. It is evident, however, that a certain temperature level exists below which no development takes place. In the experiments above described there was considerable daily fluctuation in the temperature, and hence they can be made to show only the general relation subsisting between heat and development. To find the lowest temperature at which development may go on would require thermostats in which a certain low temperature could be constantly maintained. It is probable that the shortest period of incubation might be shortened still more by placing the eggs in continuous high temperatures. We have considered this matter more in detail, because of the intimate relation between the period of development of the young tick and the so-called "period of incubation" of Texas fever.

There are some changes which the ova undergo during development which are visible to the naked eye. After a variable number of days each ovum presents a white spot. Under the microscope this corresponds to the position of the cloacal open-

ing, and is nothing else than a mass of white powder composed of very minute spherical crystals. It is an excretory product (urates?) of the young tick, the outlines of whose body and limbs are now visible through the shell under a low power of the microscope. The color of the egg itself becomes lighter, and of a more opaque, milky character. Towards the end of the period of development it assumes a peculiar metallic luster. These changes are all caused by the changes going on within the shell.

The minute six-legged ticks (Plate X, Fig. 3) after emerging from the shell are at first of a pale brownish, translucent, waxy color, which soon changes into an opaque brownish hue. They are about 0.67 mm. (.0268 inch) in length, including the mouth parts. They move actively about, carrying in their cloacal opening the chalky mass of urates (?) mentioned above. They collect along the edge between dish and cover, and scatter as soon as the cover is removed. When confined for some time in the dish, this becomes soiled with a large number of white dots discharged by the ticks.

These minute creatures are very tenacious of life when kept confined in glass dishes containing a little loam or some leaves. Young ticks hatched about the middle of December, 1890, were confined in the same glass dish in the laboratory during the winter. On May 1, 1891, four and a half months after hatching, they were still active. On May 19 a few were still active; some were inert, but not yet dead. Young ticks hatched about July 20, 1891, were still active August 29. The parasitic habit of the tick is probably so complete that no growth and no further development takes place unless the larvae gain access to cattle. When they have once attached themselves to the host and begin to get nourishment in the form of blood their growth is assured.

We have already referred to the larval and nymphal stage, so-called, as observed by Curtice. In his observations each stage occupied about a week, so that at the end of two weeks the female tick is sexually mature, prepared to become fertilized, swell up and drop off to lay her (p. 240) eggs as the beginning of another generation. When young ticks hatched within a few days of one another are placed on cattle they do not necessarily



mature at the same time. The dropping off of ripe ticks may go on some days before the animal is completely freed. In general, the time required for the tick to mature and drop off is from twenty-one to twenty-three days. These figures are the result of numerous observations made in the experiment fields at the station. The date being known when the larvae were placed on the cattle, this period was easily determined.

The life history of the tick after it has attached itself to cattle is thus easily told. Taking two weeks for the tick to become sexually mature, the fertilization takes place as described by Curtice. An examination of the skin of cattle at this time shows each female provided with a male. After fertilization the female enlarges very slowly until from the nineteenth to the twenty-second day, when she swells up very rapidly, a day or two producing great change in size. When the proper stage is reached she loosens her hold upon the skin and drops to the ground, where the laying of eggs begins in a few days. The length of time elapsing between successive generations of ticks may be tabulated approximately as follows:

	<i>days</i>
From oviposition to the larval state (period of incubation).....	20 to 45
From larval to adult state (parasitic stage).....	<u>21 to 23</u>
Age of one generation.....	41 to 68

It should be borne in mind that the young, after emerging from the egg, may perhaps live on the fields an indefinite length of time before they gain access to cattle. We have kept them alive for several months. How they would fare under the varying conditions of moisture and dryness and of a fluctuating temperature we are unable to state, from lack of observation. This free-living period must be added to the total given above to obtain a more accurate idea of the life of a single generation. Yet it is of little importance and without doubt very brief, for when cattle are within accessible distance the young ticks soon find their way to their host.

The problem how the tick passes the winter is an important one which needs special investigation. In the warmer climates

ticks are found on cattle during the winter season, and hence the development from the egg goes on during the entire year. It is highly probable that in those regions where the temperature falls too low for the tick to live on cattle the species is carried through the winter in the ovum. The great vitality of the ova is illustrated in the following experiment:

A number of dishes containing eggs were placed in a cold store-room in the attic of the Department building during November and December, 1890, and January, 1891. The eggs were placed on the bottom of the dishes, which, otherwise empty, were covered with glass covers. They were occasionally inspected in the course of the winter and early spring, but not thereafter until July 15, 1891. It was then found that in three out of nine dishes (one placed there in November, one in December, and one in January) the embryos had developed and hatched at the approach of hot weather, but were now dead. The young ticks had left behind the little chalky masses of urates (?) over the inner surface of the dishes. In the other dishes the eggs were shriveled. Signs of development were absent. This shows that the ova lived through the winter under unfavorable conditions of moisture, since the air of the room was quite dry. The capacity of the tick to survive (p. 241) occasionally the winter in regions north of its natural habitat was demonstrated in an unexpected manner on the station grounds in 1891. In September of 1890 ticks hatched in the laboratory were placed on two cows in a piece of woodland belonging to the station, but some distance removed from it. These contracted the disease in due time. One died during the acute attack, the other succumbed after it. The ticks matured from this case, wintered over, probably, among the leaves under the trees, and on September 1, 1891, one young animal in this inclosure was found with many ticks attached to it, and the examination of the blood demonstrated Texas fever. The other animals in the inclosure were insusceptible Southern animals, kept over from previous years, but likewise infested with ticks. Since it is quite impossible that any ticks could have been taken to this inclosure during the summer of 1891, the explanation given above is the only admissible one. The ticks did not reappear in 1892.

Aside from the relation which the tick bears to Texas fever as the carrier of the microorganism of this disease, it is pertinent to inquire in this place what other injury this parasite might inflict on cattle. That it abstracts a certain quantity of blood during the later days of its parasitic existence is evident. The intestine is distended with a dark-red, tarry, viscid mass, from which an abundant crop of haemin crystals may be obtained according to the well-known method of adding a crystal of common salt and some glacial acetic acid to some dried contents of the tick's body cavity on a glass slide and heating the latter until bubbles of gas are given off. These crystals show that there is much concentrated coloring matter of the blood corpuscles in the body of the tick. Yet it is doubtful whether in the aggregate very much blood is abstracted by the ticks, and the various cases under observation did not warrant the conclusion that any marked impression was made on the number of red corpuscles of insusceptible or recovered cases.

The tick produces more or less inflammation of the true skin and subcutis where it is attached. Sections of skin examined under the microscope show a very intense cell infiltration at the place of attachment, and for several millimeters around it. This infiltration is not noticed by the unaided eye. It is probable that it is due to the irritation caused by certain unknown secretions of the tick, which aid it in working its way through the upper layers of the skin and in obtaining blood in an uncoagulated state from the blood vessels attacked by it. After having attached themselves, ticks are in communication with blood vessels, for in removing them a drop of blood oozes from the place of attachment.

The young ticks attach themselves by preference to the more tender regions of the hide, such as the inner aspect of the thighs, the pubic region (escutcheon), and around and on the udder. When numerous they may attach themselves to the neck, the sides of the thorax, the ears, and even the back. In searching for them the regions first mentioned must be thoroughly examined. It must also be borne in mind that when the disease appears the ticks are still quite small and may be overlooked.

Even at the time of death only a small number may have passed beyond the second molt. The ticks still within the second skin are only 3.2 mm. (about one-eighth inch) long. Those just emerged are of the same length. The more active males of the same stage are only 2 mm. (one-twelfth inch) long. The largest ticks found on animals which die during the acute attack are not more than 5 to 8 mm. (one-fifth to one-third inch) in length. When ready to drop off (p. 242) from insusceptible or recovered cases, they are about half an inch long (12 mm. long, 7 mm. broad, and 4 mm. thick).

In the foregoing it has been stated that the female tick remains until maturity upon the same animal to which it attached itself after emerging from the egg. Each tick, in other words, is parasitic upon but one animal. What becomes of the ticks not yet matured, which are attached to the skin of natives when the latter succumb to Texas fever, we can not state definitely. It is certain that they do not at once leave the dead body, for in the case of cattle which die early in the night the ticks are still found attached next morning. In the case of a calf kept in a large refrigerator several were found attached forty-eight hours after death. If ticks are removed by the hand from the dead body it will be found that the males as well as those females which have passed through the second molt move about with some show of activity, while those individuals which have not yet cast off the molted skin are motionless. Taking these facts into consideration, we must regard the movement of ticks from one animal to another as an unnatural process which, so far as we know, may take place, but which from general observation does not appear to be of much importance. Still, it is nevertheless desirable that experiments be made to determine positively whether ticks may be transplated after the last molt, and whether at this advanced stage in their life history they are still capable of producing Texas fever.

Paquin states (9, p. 45) that full-grown ticks contain the "bacteria" of Texas fever. In order to see whether ticks contain bacteria, and what kind, the following inoculation experiments were made:

(1) July 7, 1890.—A large North Carolina tick was taken and its back scorched through with a red hot platinum spatula, thus exposing the body cavity. A loop of the black tarry contents transferred to peptone bouillon. A coccus, arranged in the form of tetrads, produces a faint cloudiness and a deposit in the inoculated tube.

(2) A second tick from the same source treated in the same way. The culture contains a coccus of the same form.

(3) July 10, 1890.—From a large tick from Texas cattle a peptone bouillon tube inoculated. Remains sterile.

(4) Another large Texas tick used. The resulting peptone bouillon culture contains a flocculent growth of large bacilli in chains.

(5) July 18, 1890.—An agar tube inoculated from a large tick, as before. Remains permanently sterile.

(6) Another agar tube inoculated from another tick. A considerable number of small colonies develop, having an opaque center and translucent periphery. They are made up of short bacilli.

(7) A peptone bouillon tube inoculated from a large tick becomes clouded with large motile spore-bearing bacilli.

These experiments show that the tick may harbor a variety of bacteria or none at all.

#### FIELD EXPERIMENTS TO DETERMINE THE PRECISE RELATION BETWEEN THE CATTLE TICK AND TEXAS FEVER

These experiments were begun in the summer of 1889, and have been continued up to the present. They have been carried on in three different directions:

(1) Ticks were carefully picked from Southern animals, so that none could mature and infect the ground. The object of this group of experiments was to find out if the disease could be conveyed from Southern to Northern stock on the same inclosure without the intervention of ticks.

(2) Fields were infected by matured ticks and susceptible cattle placed on them to determine whether Texas fever could be produced without the presence of Southern cattle.

(p. 243) (3) Susceptible Northern cattle were infected by placing on them young ticks hatched artificially, i.e., in closed dishes in the laboratory.

These three lines were not followed simultaneously, because, for instance, the fact that the disease can be produced by placing young ticks on cattle was discovered in 1890, and hence only tried then and thereafter. In giving the details of the various experiments we shall adhere not to the classification given above, but rather to the chronological order in which the experiments were performed. This is necessary in order to describe successively the experiments of the same year, which were more or less connected with one another, and also to show the process by which the various facts concerning the cattle tick came to our knowledge.

The disease was introduced into one field each year by North Carolina cattle brought here for this purpose. In 1890 a field was infected by cattle from Texas.

The field experiments were all conducted on the experiment station of the Bureau of Animal Industry, within half a mile of the limits of the city of Washington. The arrangement of the various experimental fields is shown for each year on a plat of the station grounds. The isolated condition of the field in use in any given season may be seen by an inspection of these plats. They are either separated from one another by a piece of ground remaining permanently free from infection, or by a lane or by a strip of ground purposely fenced off between them. No two fields in use are thus separated merely by a fence. In every case, with the exception to be noted, a strip of ground intervenes which is at least 36 feet wide. A small brook passes through a portion of the grounds, as is shown in the various plats, and the space between the fields along this brook is about 20 feet wide.

#### EXPERIMENTS OF 1889 (FIRST SERIES)

To carry on the experiments in the early part of the season of 1889, seven head of cattle were collected in Craven County, N. C., which is a portion of the permanently infected territory. On June 25 they were shipped by steamer from New Berne, N. C., and they arrived at the station near Washington June 27. They had thus been two days on the way. These animals were rather thin and a large number of cattle ticks (*Boophilus bovis*) in various stages of development were attached to them. Only a few were full grown.

*Experiment 1 (exposure to Southern cattle with ticks).*—Of these seven head four were placed in field I (see Fig. 4) on the day of arrival, June 27. The field contains about nine-sixteenths of an acre. The soil is a dry, gravelly loam. A small stream passes through it, from which the cattle obtain their drinking water.

The history of the native cattle placed in this field may be briefly summarized.

(a) North Carolina cattle with ticks:

No. 12, placed in this field June 27, removed August 17.

No. 40, placed in this field June 27, removed August 17.

No. 42, placed in this field June 27, removed August 17.

No. 45, placed in this field June 27, removed August 17.

(b) Native cattle:

June 27.—No. 7 (cow, 6 years) placed in this field. Dead\* August 23.

June 27.—No. 8 (cow,  $1\frac{1}{2}$  years) placed in this field. Killed† August 27.

(p. 244) June 27.—No. 75 (calf of No. 8, 4 months) placed in this field. Recovered.

June 27.—No. 9 (bull,  $1\frac{1}{2}$  years) placed in this field. Died August 31.

June 27.—No. 10 (calf of No. 7, 4 months) placed in this field. Died August 31.

June 27.—No. 11 (calf of No. 7, 4 months) placed in this field. Killed Sept. 10.

August 20.—No. 46 (heifer,  $1\frac{2}{3}$  years) placed in this field. Killed Sept. 10.

August 24.—No. 43 (steer, 3 years) placed in this field. Dead September 13.

August 24.—No. 44 (steer, 4 years) placed in this field. Dead September 17.

September 6.—No. 53 (heifer,  $1\frac{1}{2}$  years) placed in this field. Recovered.

September 6.—No. 54 (heifer, 2 years) placed in this field. Killed September 20.

\* Unless otherwise stated the cause of sickness and death is Texas fever.

† With one exception (No. 163) all native animals reported killed in this report were in a dying condition at the time.

September 14.—No. 57 (cow, 9 years) placed in this field. No result.

September 30.—No. 70 (steer, 2½ years) placed in this field. Died October 19.

October 19.—No. 71 (heifer, 3½ years) placed in this field. Probably no disease.

The disease in this field was designed to furnish material for general investigation as well as to serve as a control for experiment 2 below. (p. 245) It illustrates admirably a number of important characters of this remarkable disease and demonstrates once again the frequently observed fact that cattle, to all appearances healthy, may become the cause of an extensive fatal disease when transferred in the warmer seasons of the year from a certain permanently infected area to territories north of this area.

The first high morning temperature appeared August 15, or thirty-nine days after the native and Southern cattle were placed on this field together. The first death occurred August 23, or forty-seven days after this same date. In other words, the cattle exposed at this time died not less than forty-seven days after the beginning of the exposure. After a certain time, however, death follows more speedily after exposure, as may be seen when we consult those cases exposed August 20 and thereafter, for which this period was only fourteen to twenty-three days. The field remained infected so as to caused death as late as October 19. The later the exposure the less likely is the disease to end fatally.

Omitting the last case, No. 71, as having been exposed too late, we have ten deaths from thirteen cases exposed, or 76.8 per cent. It should be noted that, although the Southern cattle were removed from the field August 17, the infection on the field remained unimpaired.

*Experiment 2 (exposure to Southern cattle without ticks).*—For this experiment, field II was selected (see Fig. 4). The soil is the same as that in field I, but there is no running or standing water in it. It contains one-third of an acre.

This experiment differed from the first in that the *ticks* were



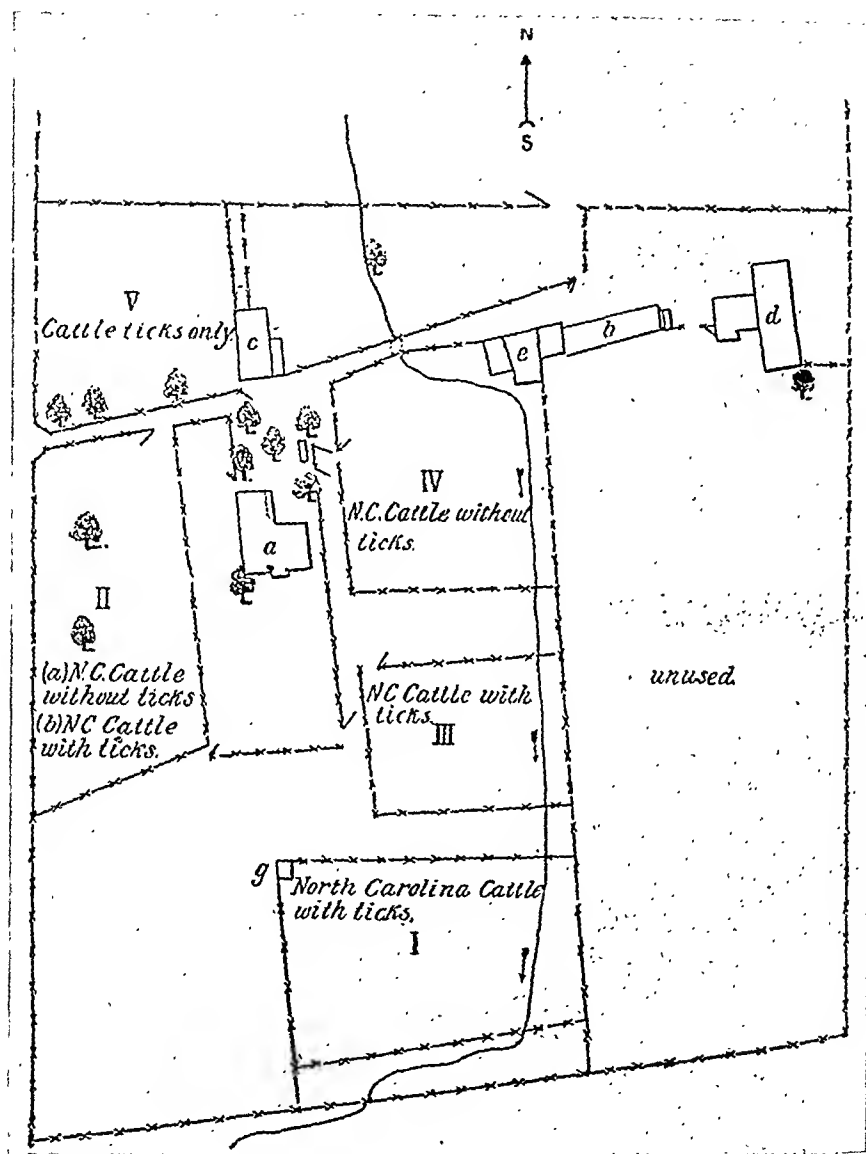


FIG. 4. FIELD INCLOSURES FOR 1889

Scale,  $\frac{1}{4}$  inch = 33 feet. *a*, dwelling house; *b*, station laboratory; *c*, horse stable; *d*, cow stable; *e*, breeding pens; *f*, tool house; *g*, shed in field.

*carefully picked from the three North Carolina cattle left after stocking field I.* The picking was done by hand. On July 6 and 17 the cattle were again carefully inspected, and any ticks which had thus far escaped attention were carefully removed. On July 23 no more ticks could be detected. In this way it was expected that no ticks would mature and infect the field. The following cattle were placed in this field June 27, 1889:

(a) North Carolina cattle without ticks, Nos. 28, 29, and 30.

(b) Native cattle: No. 51 (cow, 3 years); No. 52 (calf of No. 51, 4 months); No. 53 (heifer, 1½ years); No. 54 (heifer, 2 years).

On September 6, no ticks and no disease having appeared in this field, Nos. 53 and 54 were transferred to field I. Their further history is given under experiment 1. It would have been more satisfactory to have left these animals on this field until the close of the season of 1889. But the evidence is decidedly in favor of the assumption that there was no infection of these animals when they were transferred to the infected field. This evidence is twofold: (1) The three adult animals and one calf in control field I were dead by August 31, and the remaining calf was killed in a dying condition September 10. Hence all five animals exposed at the same time in the field containing ticks were either dead or very sick on the date of the removal of these two to field I. They on the other hand were at this time to all appearances healthy. (2) One transferred case (No. 54) was dying of an acute attack September 20, as the autopsy notes and microscopical observations demonstrate. If this animal had been affected September 6, at the time of transfer, the blood corpuscles would have shown later on enlarged and stained forms (macrocytes) always associated with prolonged disease. No. 53 first showed external signs of disease in the last week of September, at which time it lost much flesh and was very weak. In October it was passing through a mild or secondary attack. Both transferred (p. 246) animals, therefore, must be regarded as having contracted Texas fever after September 6, on field I. The same arguments apply to Nos. 51 and 52 which were re-exposed later on in the season (experiment 4).

## EXPERIMENTS OF 1889 (SECOND SERIES)

In September of 1889 a second series of experiments were carried on in order to repeat the observations on the relation of ticks to Texas fever. Nine head of cattle were collected in Craven County, N. C. Three were taken from each of three farms located several miles from New Berne, and in opposite directions from that city. The three cattle from one farm were shipped from New Berne September 10, and reached the station September 14. The remaining six were shipped September 12, and arrived September 15. The three of the lot to arrive first were placed in their respective fields a day earlier than the remaining six. All cattle were well loaded with cattle ticks, many of which were nearly matured.

*Experiment 3 (exposure to Southern cattle with ticks).*—For this experiment field III was chosen (see Fig. 4). It resembled field I in having a running stream and contained about three-eighths of an acre. It was separated from field I by a lane 36 feet wide. The experiment was designed as a control to the others below, and in order to insure the same conditions in every respect one of each of the three lots of cattle was placed in it. The following animals were in this field:

(a) North Carolina cattle with ticks:

No. 113, placed in field III September 14.

No. 60, placed in field III September 15.

No. 62, placed in field III September 15.

(b) Native cattle:

No. 35 (heifer, 2 years), placed in field III September 14.

No. 47 (cow, 3½ years), placed in field III September 14.

No. 49 (heifer, 3 years), placed in field III September 14.

Of these three natives only No. 47 passed through a severe attack of the disease, as the notes in the case demonstrate. The season was somewhat too far advanced when the exposure began, and of the new generation of ticks only very few appeared on the native cattle afterward.

*Experiment 4 (exposure to Southern cattle with ticks).*—This

experiment is the counterpart of experiment 3, excepting that it was conducted in field II, which is without running water. Field II, moreover, was occupied by Southern cattle without ticks in July and August, as will be seen by referring to experiment 2. From this experiment there remained in the field natives Nos. 51 and 52. On September 14 and 15 three North Carolina animals, one from each of the three lots, were placed in this field, and one native, No. 56, was added September 14. There were, therefore, in this field on September 15—

(a) North Carolina cattle with ticks, nos. 32, 61, and 67.

(b) Native cattle:

No. 51 (from experiment 2). Passed through the disease and recovered.

No. 52 (from experiment 2). Passed through the disease and recovered.

No. 56 (steer, 2½ years). Probably not affected.

On October 9, ticks had almost entirely disappeared from the Southern cattle, and very few young ticks subsequently appeared on the natives.

*Experiment 5 (exposure to Southern cattle without ticks).*—For this experiment field IV was chosen (see Fig. 4). It covers about three-eighths (p. 247) of an acre, is situated above field III, and separated from it by a lane 36 feet wide. The stream passes through it on the east. Three Southern cows, one from each lot, were placed in this field after the ticks had been carefully picked off so far as they could be seen. In this field there were the following animals:

(a) North Carolina cattle without ticks:

Nos. 55, 59, and 63, the first put on the field September 14, the others September 15.

(b) Native cattle:

No. 41 (heifer, 4 years), placed in this field September 14.

No. 50 (cow, 3 years), placed in this field September 14.

No. 97 (calf of No. 50, 2 months old), placed in this field September 14.

No. 66 (heifer, 1½ years), placed in this field September 14.

The Southern cows were reëxamined September 18, 23, October 1 and 9, and some remaining ticks removed. On October 9, only two or three were found. Up to November 27 no ticks were detected on the native cattle, and no symptoms of disease were noticed.

*Experiment 6 (exposure to cattle ticks only).*—This experiment was carried on in field V, an inclosure consisting of about three-eighths of an acre. The soil is a heavy clay loam, and contains neither running nor standing water. On September 13 several thousand, mostly full-grown ticks, were scattered over the ground in this field. These ticks had been collected from cattle near New Berne, N. C., September 9 and 10. There were placed in this field, September 14, four natives:

No. 48 (cow,  $2\frac{1}{2}$  years).

No. 83 (calf of No. 48, 2 months).

No. 64 (steer,  $2\frac{1}{2}$  years).

No. 65 (heifer,  $2\frac{1}{2}$  years).

Of these, Nos. 48, 64, and 65 contracted Texas fever. No. 83 was not examined as to its blood, but is showed no external symptoms of disease. No 48 was killed in a dying condition, October 21. The autopsy, as well as the examination of the blood before death, demonstrated Texas fever. Nos. 64 and 65 recovered.

#### SUMMARY OF THE EXPERIMENTS FOR 1889

The first series (Nos. 1 and 2) go far toward demonstrating that a field must be infected with ticks before Texas fever can appear among natives. The second series confirms the first as far as it goes. The advanced season gave rise only to what has been called the mild or autumnal type of the disease, characterized by the presence in the blood corpuscles of the peripheral coccus-like stage of the Texas-fever parasite. If we bring together the results of the four experiments we find that in the field containing the ticks only, and in which Southern cattle at no time entered, all three exposed adult natives took the disease. In the field containing Southern cattle from which the ticks had been picked

no disease appeared. Finally, in the two fields which contained Southern cattle and ticks together three out of six natives became diseased. In these experiments the great importance of the method of blood examinations as described in the first part of this volume is plain. To rely solely upon external symptoms in mild attacks is out of the question. The counting of the red corpuscles, the changes going on in the latter, and the presence of the Texas-fever parasite as determined by microscopical examination are indispensable in determining whether Texas fever is present or not.

(p. 248)

#### EXPERIMENTS OF 1890

The experiments of this year were chiefly occupied with the relation of ticks to Texas fever. The experiments of last year were repeated, and in addition ticks were hatched artificially and placed on cattle with the result that Texas fever appeared in every case (experiments 12 and 13). Southern cattle were obtained as before from North Carolina (Experiment 9) and also from Texas (Experiment 8).

*Experiment 7 (to ascertain whether the infection of 1889 survived the winter).*—For this purpose fields I and III of 1889 were thrown together by removing the intervening fences and the whole designated field I (see Fig. 5). The little stream was likewise fenced off in July to prevent any infection from field VI reaching it. A number of animals were pastured on this field.

(p. 249) May 26, 1890.—No. 74 (heifer, 2 years). Transferred to field II September 25.

May 26, 1890.—No. 91 (heifer, 3 years). Transferred to field VI October 1.

July 4, 1890.—(Stream fenced off, as field VI is now used for the first time).

July 9, 1890.—No. 130 (cow, 5 years).

August 25, 1890.—No. 97 (bull, 1 year).

During the summer no ticks appeared in this field, so that it was evident that they had not survived the winter. No disease appeared in any of the animals exposed.

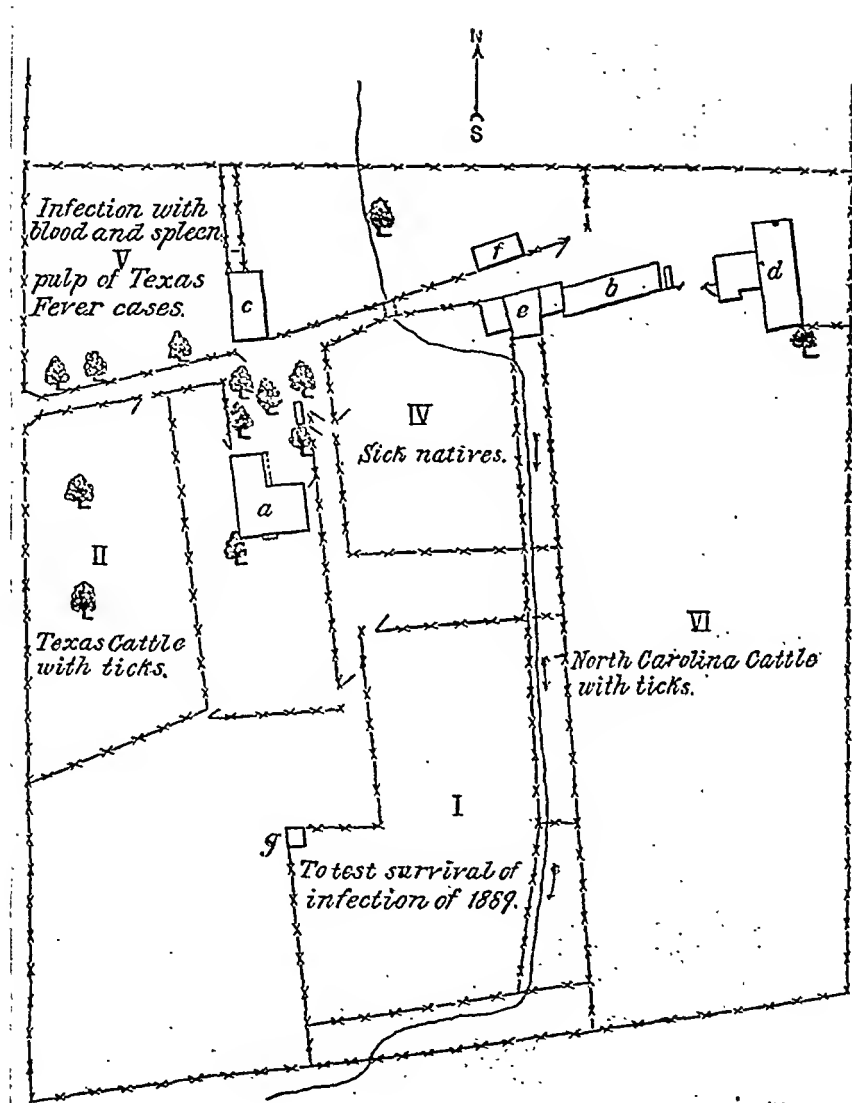


FIG. 5. FIELD INCLOSURES FOR 1890

Scale,  $\frac{1}{4}$  inch = 33 feet. For an explanation of the letters see figure 4

*Experiment 8 (to ascertain whether the disease introduced by Texas and that introduced by North Carolina cattle are the same).*—Four heifers were removed from their pasture near Houston, Tex., June 30, and sent by express to the station, where they arrived July 4. Hence, they were but four days off the Southern pasture before they were placed in field II (see Fig. 5). The heifers were in rather poor condition and all well supplied with cattle ticks of all stages. The field corresponded with field II, of 1889, but it was slightly enlarged so as to include about  $\frac{1}{16}$  of an acre. The field thus contained—

(a) Texas cattle with ticks:

No. 124 (heifer, 2 years).

No. 125 (heifer, 3 years).

No. 126 (heifer, 4 years).

No. 127 (heifer, 5 years). All placed in field II, July 4.

(b) The native cattle were exposed in the following order:

July 4.—No. 128 (cow, 12 to 14 years). Dies September 1.

July 5.—No. 80 (cow, 7 years). Killed August 28.

July 5.—No. 82 (calf, 5 months). Diseased, but recovered.

July 5.—No. 107 (heifer, 1 year). Diseased, but recovered.

July 5.—No. 129 (heifer, 2 years). Dies August 29.

August 30.—No. 139 (cow, 6 years). Died September 13.

September 25.—No. 74 (heifer from field I). Dies October 16.

September 25.—No. 62 (N. C. heifer of 1889). Exposure negative.

As regards the cattle ticks, the following observations were made: On July 30, only a few adults were still attached to the Texas cattle, the rest having disappeared. On October 20, only very few young ticks were still found on the surviving cattle, and eight days later they had all disappeared.

Any differences between the disease in this and the North Carolina fields could not be found.

*Experiment 9 (exposure to North Carolina cattle with ticks. General control field for 1890).*—Field VI was chosen for this purpose. It covers  $1\frac{1}{2}$  acres, and is fenced off from the stream. Between it and the other fields (I, IV) is a strip of land containing the stream bed. To carry on the various experiments of the



year, and to infect this field, cattle were taken from North Carolina fields as in 1889. The cattle were collected July 1, shipped by steamer from New Berne, N. C., July 2, and received at the station July 4. Of those received, the following were placed in field VI on July 4.

No. 114 (heifer, 2 years), from North Carolina; farm 1.

No. 112 (old cow), from North Carolina; farm 4.

No. 120 (cow, 7 years), from North Carolina; farm 2.

No. 119 (calf of No. 120, 3 months), from North Carolina; farm 4.

No. 121 (cow, 3 years), from North Carolina; farm 4.

No. 122 (heifer, 2 years), from North Carolina; farm 3.

These Southern animals were in fair condition, excepting No. 112, which was very thin and weak. All excepting No. 114 were well supplied with cattle ticks.

(p. 250) The following Northern animals were placed in field VI:

July 4.—No. 49 (cow, 4 years), exposed in 1889, but probably not affected at that time.

July 4.—No. 85 (calf of No. 49, 3 months).

July 4.—No. 50 (cow, 4 years), in field IV in 1889, but not affected.

July 4.—No. 57 (cow, 10 years), exposed in field I in 1889, but probably not affected.

July 4.—No. 79 (calf of No. 50, 3 months).

July 4.—No. 66 (heifer, 2 years), exposed in field IV in 1889, but not affected.

July 4.—No. 69 (cow, 3 years).

July 4.—No. 100 (calf of No. 69, 2 months).

July 4.—No. 95 (cow, 4 years).

July 4.—No. 93 (calf of No. 95, 1½ months).

August 13.—No. 71 (heifer, 4½ years) transferred from field I.

August 13.—No. 134 (heifer, 2 years).

August 25.—No. 90 (bull, 1 year).

September 8.—No. 56 (steer, 3½ years), exposed in field II in September, 1889, but probably not affected.

These various animals (excepting Nos. 49, 56, and 57) may be regarded as unexposed natives, although some of them had been used the year previous and early in this season in fields presum-

ably free from infection. The result of the exposure may be tabulated as follows:

No. 49 has a severe attack but recovers.

No. 85 has a mild attack.

No. 50 dies September 6, sixty-four days after the beginning of the exposure.

No. 57 is not affected.

No. 79 has a very mild attack and recovers.

No. 66 dead September 1, fifty-nine days after the beginning of the exposure.

No. 69 dies September 3, sixty-one days after the beginning of the exposure.

No. 100 has a mild attack, but succumbs in December.

No. 95 killed in dying condition, August 25, fifty-two days after exposure.

No. 93 has a mild attack.

No. 71 dead September 6, twenty-four days after beginning of exposure.

No. 134 killed in dying condition August 28, fifteen days after exposure.

No. 90 dies September 16, twenty-two days after exposure.

No. 56 has a prolonged but mild attack and recovers.

It will be seen from this table that all animals exposed in mid-summer (July and August) died or were killed in a dying condition, excepting the calves. These were all affected; one died in the fall and one was killed, but in every case the attack was mild. The mortality among those over 1 year old was 80 per cent. It will be noticed also that animals exposed in August died with those exposed a month earlier. Those exposed on July 4, when the field was first infected, died from fifty-two to sixty-four days thereafter. Those exposed in August died in fifteen to twenty-four days after the first day of exposure.\*

On July 30 only a few full-grown ticks were left on the Southern stock. August 13, two weeks later, young ticks had appeared

\* In this field there were placed during the summer some animals which had passed through one attack of the disease, and some Southern animals kept on the station from the year previous. These cases will be reviewed under another subject.

on all the cattle, native and Southern alike. August 25 some of these had become full grown. In the middle of October only a few young ticks could be seen, and by the end of the month they had practically disappeared.

*Experiment 10 (exposure to cattle ticks only).*—Field VIII was used in this experiment. (See Fig. 6.) It is a fenced off portion of a piece of ground situated about one-fourth mile north of the station grounds upon which the experiments thus far recorded were carried on. This particular field covers about  $1\frac{3}{8}$  acres, and is separated from the adjoining field VII and IX by strips of ground as shown in the plat. The ground (p. 251) is covered largely with trees (oak and chestnut) and may be regarded as sparsely wooded. It slopes toward field VII at an angle of  $20^{\circ}$ – $30^{\circ}$ . On July 4 about 4,000 matured and 1,000 half-grown ticks were scattered over the ground in this inclosure. The ticks had been collected between June 28 and July 2, about New Berne, N. C., and placed in a large can containing grass from Washington station. At the time they were scattered over the field many had already laid a portion of their eggs.

In this field were placed the following native cattle:

July 4.—No. 76 (heifer, 1 year).

July 4.—No. 102 (cow, 6 years). No. 102<sup>a</sup> (calf of No. 102, born on this field September 1).

July 4.—No. 105 (heifer, 2 years).

August 21.—No. 47 (cow,  $4\frac{1}{2}$  years, recovered case of 1889).

August 21.—No. 135 (heifer, 2 years).

(p. 252) The result of the exposure is briefly as follows:

No. 76 killed in dying condition August 18.

No. 102 very sick with Texas fever, but recovered.

No. 102<sup>a</sup> died of Texas fever thirteen days after birth.

No. 105 very sick, but recovered.

No. 47\* died September 12.

No. 135\* very sick, but recovered.

\* These cases were transferred subsequently to an uninfected field in order to determine whether they could communicate the disease to other natives.

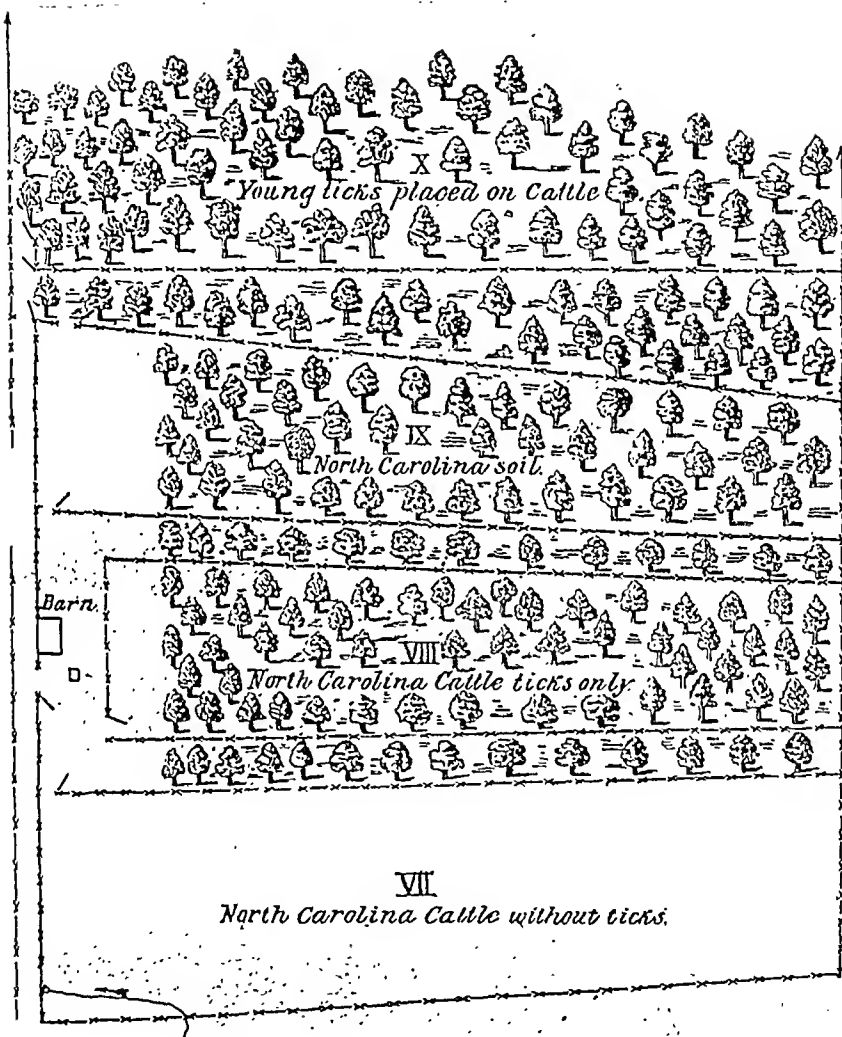


FIG. 6. SUPPLEMENTARY INCLOSURES FOR 1890  
Scale,  $\frac{1}{4}$  inch = 33 feet

Of the six cases exposed to the ticks only, all were unmistakably affected with Texas fever, as the notes recorded show. Three died and the autopsy confirmed the diagnosis. The reason why the mortality was not so high here as in the preceding experiment is probably to be sought for in the fact that under natural conditions the young ticks appear more successively, and cause a more prolonged infection, while in this experiment they probably appeared nearly all at the same time.

The young ticks were seen in this field August 8, and on August 23 full-grown specimens were found on No. 102.

*Experiment 11 (exposure to Southern cattle without ticks).—*This experiment was conducted on field VII, adjoining the field of the preceding experiment. (See Fig. 6.) It covers about  $1\frac{3}{4}$  acres, and contains both running and standing water from a spring. It is not wooded. The following Southern cattle brought from North Carolina (with those placed in field VI of this year) were put into this inclosure after all ticks that could be found were carefully removed:

July 4.—No. 115 (cow, 6 years) from farm 4.

July 4.—No. 116 (heifer, 2 years) from farm 2.

July 4.—No. 117 (heifer, 2 years) from farm 3.

July 4.—No. 118 (cow, 10 years) from farm 4.

July 4.—No. 123 (heifer, 3 years) from farm 1.

Into this inclosure were placed on the same day the following native cattle: No. 103 (heifer, 3 years); No. 106 (heifer, 2 years); No. 108 (heifer, 2 years).

The Southern cattle were reexamined three times a week between July 7 and July 28, to remove any ticks which on account of their small size had escaped detection. On a final examination July 30 no more could be found.

Nevertheless, on August 15, a few young ticks were found on the natives, and three days later a large number had attached themselves. The outcome was the death of the three natives. No. 103 died August 28; No. 106 died September 6; No. 108 died September 9.

The experiment had thus failed in so far as ticks had not been kept out of the field. Although it is not to be denied that some may have escaped attention and fallen to the ground, yet it is highly probable that most if not all the ticks or their eggs were washed in from the adjoining field VIII, which is considerably higher and slopes toward VII. There had been exceptionally heavy showers August 1 and August 8, which had carried much soil, and even stones as large as a fist, into this field. At all events, this difficulty might have been avoided by reversing the location of the two experiments and placing the animals free from ticks on the higher ground.

*Experiment 12 (production of Texas fever by placing on native cattle young ticks artificially hatched in the laboratory).*—Hitherto we had supposed that the cattle tick acts as a carrier of the disease between the Southern cattle and the soil of the Northern pastures. It was believed that the tick obtained the parasite from the blood of its host, (p. 253) and in its dissolution on the pasture a certain resistant spore form was set free, which produced the disease when taken in with the food. The feeding of one animal (No. 145) for some time with grass from field VI, the most abundantly infected of all, without any appearance of disease made this hypothesis untenable. But even before this feeding experiment was undertaken other facts were noticed which militated against this hypothesis, and which proved that the young tick calls forth the disease. In the first place, animals exposed when the field was first infected did not die until fifty to sixty days after the beginning of the exposure, while those exposed thirty or more days later on the same ground died in fifteen to twenty-five days thereafter. In the second place, all animals which succumbed had young ticks on them. In other words, the appearance of the disease was in some manner associated with the appearance of the new generation of ticks. Even with this fact fairly well determined, the true explanation that the young ticks were directly responsible for the disease seemed too far-fetched to deserve attention until it was demonstrated in the following manner. A yearling heifer had been placed in a box stall and a

number of young ticks, hatched artificially in glass dishes, had been placed on this animal at intervals, beginning August 14, in order to determine whether ticks in the capacity of blood-sucking parasites made any impression on the number of blood corpuscles. It was found by a periodical estimation of the number of red corpuscles that after a certain time this number fell so quickly and so markedly as to be wholly incommensurate with the small amount of blood abstracted by the ticks. At the same time other symptoms of Texas fever appeared and the parasite was detected in the blood.

The experiment was repeated on several other animals as soon as young ticks could be obtained.

No. 140 (heifer, 2 years old) kept in a box stall on a neighboring farm. The young ticks 3 to 4 days old were placed on it September 9. It was found dead October 2. Both blood examination during life and the autopsy demonstrated Texas fever.

No. 137 (heifer, 1 year old) was placed in field X, a wooded lot to which no infected cattle had been admitted, and on September 9 young ticks were placed on it. It passed through a severe attack of Texas fever and was killed in a dying condition November 6.

No. 144 (cow, 8 years old) was also kept in field X. The young ticks were placed on it September 17 and it was found dead October 3. In this case also the nature of the disease was beyond question.

*Experiment 13 (production of Texas fever in the winter season by placing young ticks on cattle kept in an artificially heated stable).—*The result of experiment 12 was so important that it was deemed best to repeat it in an artificially heated stable, as the season was too far advanced for ticks to thrive in the open air. The stable was warmed by means of a coal stove. The temperature fluctuated between 65° and 80°F.

This experiment demonstrates that Texas fever may be produced at any season of the year if the conditions are fairly favorable; if, in other words, the temperature of the air is sufficiently elevated to permit the cattle tick to carry on its parasitic existence. Of five presumably susceptible animals infected with ticks three showed well-marked symptoms of Texas fever, and

the remaining two reacted with a high temperature for a few days. In these latter cases there may have been a reduction in the number of red corpuscles also, but we can not regard such reduction demonstrated until the number falls below 5,000,000.

(p. 254) The following animals were exposed and infected with young ticks:

No.	Age, etc.	Placed in stable	Infection with ticks	Number of infections	Result
143	Heifer, 1½ years.....	Oct. 27, 1890	Oct. 28–Nov. 8....	2 (200–300 each time).....	Slight if any effect.
145	....do.....	....do....	Nov. 21–Dec. 3.	7 (200–300 each time).....	Prolonged case of Texas fever. Recovered Mar. 18, 1892.
149	....do.....	....do....	Oct. 28–Nov. 21.	6 (15 each time)	Slight, if any effect.
117*	Southern heifer, 2 years.	Nov. 19, 1890	Nov. 21–Dec. 3...	7 (200–300 each time).....	Do.
130	Cow, 2 years	Dec. 12, 1890	Dec. 13–Dec. 29.	9 (200–300 each time).....	Marked case of Texas fever. Recovered Feb. 18, 1891.
152	Cow, 4½ years	....do....	....do....	9 (200–300 each time).....	Mild case of Texas fever. Recovered Jan. 20, 1891.

\* In stall with No. 145.

The young ticks placed on Nos. 117, 143, 145, and 149 were descended from adults picked from diseased natives (Nos. 137, 138, and 140). Those placed on Nos. 130 and 152 were descended from adults received directly from North Carolina.

In these cases the high temperature appeared generally in fifteen days after the first lot of young ticks had been put on the animal. In No. 145 the period of marked destruction of red corpuscles was associated with high fever.

This experiment does not definitely prove that the progeny of ticks collected from susceptible Northern animals which have passed through the disease may produce as severe an attack as those descended from ticks picked directly from Southern animals. The positive result in No. 145, infected with "Northern" ticks, is vitiated by the fact that this animal was in the same stall with a Southern cow, No. 117. The severe secondary attack



appeared in No. 145 in the middle of January. This would allow time for the ticks to mature on No. 117, and the next generation to attack No. 145. Hence No. 145 may actually have received the severe secondary infection from "Southern" ticks, in so far as they were descended from those matured on No. 117. This interpretation may be wrong and the secondary infection in No. 145 may have been a true relapse resulting from the primary infection with "Northern" ticks. The experiment as it stands, however, can only be interpreted as showing that ticks produce well-marked disease in artificially-heated stables in winter, and the other question, whether "Northern" ticks may do this, must be left open.

#### SUMMARY OF THE EXPERIMENTS OF 1890

The discovery of 1889 that ticks also are sufficient to infect a field was confirmed this year. The experiment designed to test the theory that Southern cattle are infectious only through the ticks they carry failed this year, for the field became infected with ticks after all. (p. 255) Lastly, the demonstration of the important fact that the infection is conveyed by the young tick, and is probably introduced by it into the blood, was a very great stride in advance in our understanding of the external characters of the infection.

In field IX (see Fig. 6) several natives were exposed to North Carolina soil without becoming diseased.

On the station grounds field V (see Fig. 5) was infected with the blood and spleen pulp of cattle which had succumbed to Texas fever. The exposed natives did not become infected.

In field IV (see Fig. 5) during this same year a number of sick natives were brought together and some healthy natives added. The latter had a mild attack late in the season, only detected by the microscopic examination of the blood.

These three experiments will be fully discussed farther on, and we simply refer to them here to show that the animals not exposed under certain conditions did not become infected, although pastured not far from Texas-fever cases during the summer.

## EXPERIMENTS OF 1891

The arrangement of the fields for this year and the uses to which they were put are indicated on the accompanying plat. A tract of land adjoining the station grounds on the north was added to the territory in use. On this tract were situated a dwelling house and a number of unused sheds. For the purpose of carrying on the various experiments, cattle were collected near New Berne, N. C., as in previous years, and shipped by steamer from New Berne, June 30. They arrived at the station July 2, having been but two days on the way.

*Experiment 14 (exposure to North Carolina cattle with ticks).—*The general control experiment of producing the disease in the natural way was conducted, as before, by exposing natives to Southern animals on the same field. For this purpose inclosure VI was again selected (see Fig. 7). In this experiment not only unexposed natives but also recovered natives were reëxposed to test any acquired immunity. Similarly Southern animals, kept for one or two years on the station, were reëxposed to determine any loss of immunity. These collateral experiments will be discussed in dealing with these subjects. In this place we simply summarize the results of the exposure of fresh natives.

The animals placed in this comprised the following:

(a) North Carolina cattle:\*

July 2.—No. 172 (cow, 6 years), from farm No. 6.

July 2.—No. 174 (cow, 3 years), from farm No. 5.

July 2.—No. 177 (cow, 5 years), from farm No. 3.

July 2.—No. 178 (cow, 4 years), from farm No. 2.

(b) Natives.

July 2.—No. 104 (cow, 4 years). Very sick; recovered.

July 2.—No. 159 (heifer, 2 years). Not very sick; recovered.

July 2.—No. 163 (cow, 6 years). Very sick; killed August 25.

September 1.—No. 169 (cow, 8 years). Died September 14.

September 1.—No. 181 (cow, 2½ years). Killed in dying condition  
September 19.

\* Eight animals were brought North, two from each farm, and divided equally between this and the following experiment.

September 15.—No. 184 (heifer, 2 years). Died October 2.

September 21.—No. 160 (cow, 2½ years). Prolonged attack; recovered.

September 21.—No. 187 (calf of No. 160, 4 months). Not affected.

(p. 256)

(p. 257) All animals excepting the calf were attacked by Texas fever. No. 163 was killed at the height of the fever and probably would have died. The mortality among these animals was lower than in the preceding year, the conditions being precisely the same. Among those exposed later on, the mortality was higher than among those exposed early. The ticks in this field had entirely disappeared from the Southern stock by the end of July. The young ticks had appeared in considerable numbers on all the cattle August 10, and continued to increase in number during August on all cattle alike. They had all disappeared by the last of October.

*Experiment 15 (exposure to North Carolina cattle without ticks).*—The great importance of determining whether or not the ticks are the only carriers of the infection from the permanently infected regions of the South imposed upon us the necessity of trying this experiment until it could be stated with certainty that no ticks had passed from Southern to native cattle. The experiment of 1890 (Exp. 11) had failed because young ticks had appeared on the natives in course of the summer. For the repetition of this experiment the hitherto unused inclosure XI (see Fig. 7), covering over 2 acres, was chosen. The following North Carolina cattle were put into it July 2, after the ticks had been carefully picked off: No. 173 (cow, 3 years), from farm 6; No. 175 (cow, 4 years), from farm 5; No. 176 (cow, 6 years), from farm 3; No. 179 (cow, 5 years), from farm 2.

The following natives were added at the same time: No. 161 (cow, 6 years); No. 164 (cow, 7 years); No. 167 (heifer, 3 years).

The Southern animals were reexamined daily and a few small ticks found each day until July 22. Thereafter very few were found, and after July 29 none. Nevertheless, a few adults must have escaped and dropped on the ground, for young ticks made their appearance, though in small number, in August. From

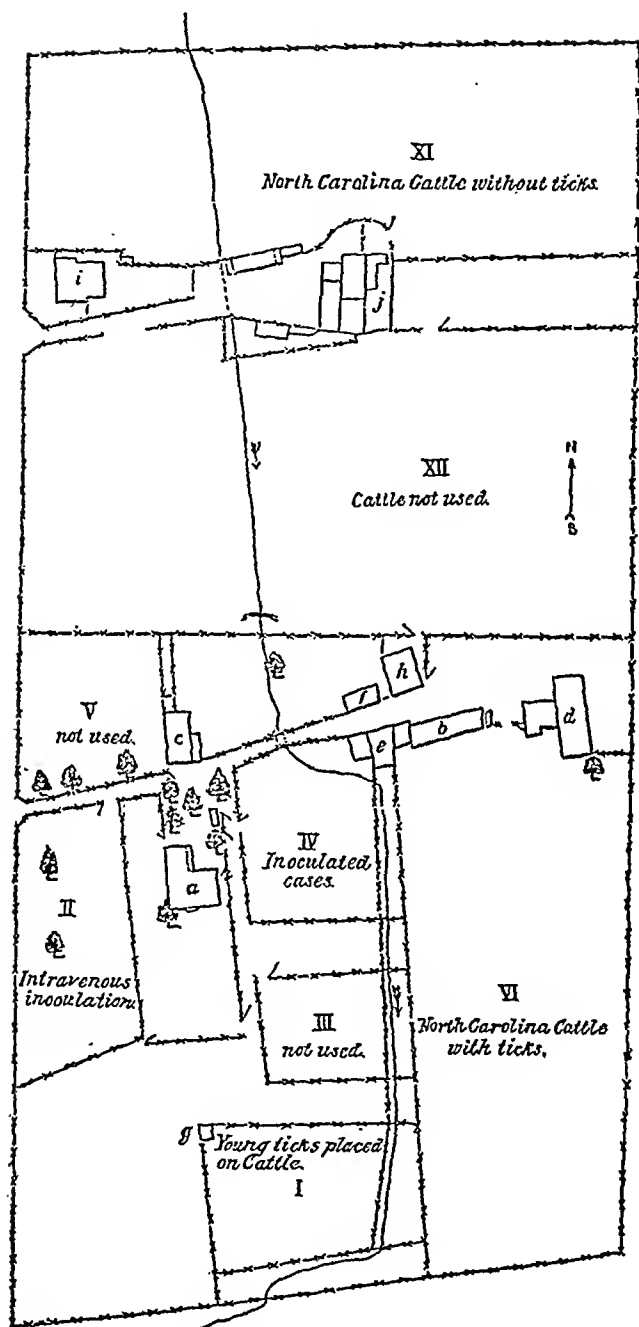


FIG. 7. FIELD INCLOSURES FOR 1891

Scale,  $\frac{1}{4}$  inch = 36 $\frac{3}{4}$  feet. *a* to *g*, as in figure 4; *h*, swine pen; *i*, dwelling house; *j*, cow stalls.

August 22 to September 3 several hundred were removed from the three natives. No. 164 was most abundantly infected. Next came 167 in this respect. No. 164 suffered a severe attack and was found dead September 3. No. 167 likewise passed through a severe attack, but recovered, while in No. 161 signs of infection were not detected, as will be seen by an examination of the notes in the appendix. The severity of the disease was thus in general proportional to the number of ticks found on these animals.

*Experiment 16 (production of disease with young ticks hatched artificially).*—This is a repetition of experiments 12 and 13 of last year, but is made much earlier in the summer. A large number of adult ticks were collected June 25–27 from cattle near New Berne, N. C. An abundance of eggs had been laid by July 7, which were placed in glass dishes containing a few fresh leaves and a few drops of water and covered snugly with a piece of glass. The young ticks began to appear July 23.

July 25, Nos. 166 and 180, both 2-year old heifers, were placed in field 1 (see fig. 7). To the rump and neck young ticks were applied daily for ten days until August 4. No. 166 received from 200 to 300 daily, No. 180 only 20 to 30 daily. After each application the heifers were held quiet for a few minutes until the young ticks had crawled away through the hairs.

July 29, No. 158, a 2-year old steer, was placed on the same field and several thousand ticks from the same lot applied at one time.

The following table summarizes the experiment:

No.	Age, etc.	Young ticks applied	Number of application	Result of exposure
166	Native heifer, 2 years.	July 23– Aug. 4.....	10 (200–300 each time).....	Severe attack; recovered.
180	.....do.....	.....do.....	10 (20–30 each time).....	Severe attack; died Aug. 12.
158	Native steer, 2 years..	July 29.....	1 (several thousand).....	Severe attack; recovered.
117	Southern heifer.....	August 30.....	1 (several thousand).	No result.

August 20, No. 117, a North Carolina heifer of 1890, was placed in the same inclosure and several thousand ticks of the same lot applied at one time. (p. 258)

In all natives a marked case of Texas fever was produced, which proved fatal in that animal to which the smallest number of young ticks had been applied. It is also interesting to note that in this experiment Texas fever appeared much earlier than in field VI (experiment 14), when the infection took its natural course. Thus in the latter field the disease was first observed August 18, while among the artificially infected it appeared as early as August 7.

#### EXPERIMENTS OF 1892

The field work of this year was mainly directed toward determining whether or not Texas fever is transmitted without ticks. The experiments of the two preceding years had failed, because young ticks appeared on the native cattle, though they had been very carefully removed from the Southern animals. This year the experiment was tried over again, and with entire success. The young ticks did not appear on the native cattle, and the latter remained free from disease in spite of the presence of North Carolina cattle. Another very important fact was demonstrated. Texas fever was produced in natives by the intravenous injection of blood from healthy North Carolina cattle, and natives exposed to these sick natives did not contract the disease, because ticks were absent.

The southern animals used in the field work of the summer were six in number, gathered together from two farms near New Berne, N. C., three being taken from each farm. They left New Berne by steamer June 29, and reached the station July 1, being off their native fields about four days before they were placed in the fields at the station.

The field inclosures for this year are numbered as they were last year. Hence the plat of 1891 (Fig. 7) will serve to illustrate the experiments to be described.

*Experiment 17 (exposure to North Carolina cattle with ticks).—*This experiment was to serve as a control upon the following ex-

periments. Field VI was again used for this purpose. Two Southern animals, one from each North Carolina farm, were introduced as sources of the infection. The contents of the field and the general results of the exposure may be tabulated as follows:

June 30, 1892.—No. 201 (cow, 5 years). Removed to uninfected field July 20; not diseased.

June 30, 1892.—No. 203 (cow, 6 years). Died of Texas fever August 22.

July 1, 1892.—No. 216 (North Carolina cow, 6 years).

July 1, 1892.—No. 217 (North Carolina cow, 6 years).

July 20, 1892.—No. 220 (steer,  $2\frac{1}{2}$  years). Very sick; recovered.

July 20, 1892.—No. 223 (heifer, 6 years). Died of Texas fever August 23.

August 26, 1892.—No. 204 (bull,  $2\frac{1}{2}$  years). Very sick; recovered.

On July 20 only a few half-grown ticks were found on the Southern cows. On August 5 the young ticks were first noticed on the natives; (p. 259) at this time they had probably been on the cattle only two or three days. The outcome of the exposure does not differ from that of preceding summers. All exposed animals contracted Texas fever, and two of the three early exposures died.

It is interesting to note that No. 201, though it was pastured on the infected field for twenty days, remained perfectly healthy, because it was removed to an unused field (IV) before the young ticks had appeared in the infected field. It is likewise worthy of notice that No. 223, though exposed twenty days later than No. 203, became infected at about the same time and died only a single day later. The reason for this has already been pointed out, but it deserves repetition. The infection of the field is established when the young ticks have hatched, and not before. Hence a field is not dangerous until twenty or twenty-five days (according to the average temperature) after Southern cattle have pastured on it.

*Experiment 18 (exposure to North Carolina cattle without ticks).*  
—Field I (see Fig. 7) was used for this test. Two North Carolina

cows (Nos. 212 and 213), one from each farm, were chosen, so as to make the conditions as nearly like those in the control field as possible, and the ticks carefully picked off before they were placed in this field. They were subsequently examined daily for any ticks too small to be seen originally. Two native cows (Nos. 208 and 209) were placed in the inclosure with them. These remained perfectly well throughout the summer.

*Experiment 19 (exposure to North Carolina cattle without ticks).*—This is an exact duplicate of the preceding experiment, to insure the success of one in case the other failed, by reason of the appearance of young ticks. Two North Carolina animals (Nos. 214 and 215), one from each farm, were carefully picked over and all ticks removed so far as they could be detected. They were placed in field No. II, July 2. Two native cows (Nos. 205 and 210) had been placed in the same field two days before. The Southern animals were carefully reexamined for ticks, as in the experiment preceding, for several weeks. In this field no disease appeared during the entire summer.

The cases in these fields may be tabulated as follows:

#### Field I

July 2.—No. 212 (North Carolina cow, 3 years).

July 2.—No. 213 (North Carolina cow, 5 years).

June 30.—No. 208 (cow, 5 years). Exposure negative (October 1).

June 30.—No. 209 (cow, 9 years). Exposure negative (October 1).

#### Field II

July 2.—No. 214 (North Carolina cow, 4 years).

July 2.—No. 215 (North Carolina cow, 4 years).

June 30.—No. 205 (cow, 5 years). Exposure negative (October 1).

June 30.—No. 210 (heifer, 2 years). Exposure negative (October 1).

#### MISCELLANEOUS EXPERIMENTS

*Experiment 20 (to test infection by way of the digestive tract).*—No. 131, a heifer, 2 years old, was placed in a box stall July 29, 1890, and fed at three intervals about 2,000 adult live ticks in all. The animal remained well. No blood examinations were made.

No. 110, a heifer, 1 year old, was placed in a box stall August



14, 1890, and fed several thousand young ticks and egg cases. The result was to all appearances negative. Unfortunately the blood was not examined.

(p. 260) No. 145, a heifer, 18 months old, was placed in a box stall September 17, 1890, and fed once daily with one-fourth bushel of grass cut from the infected field VI, together with hay and mill feed. The experiment was closed October 12. No indications of disease during the feeding or until November 21, when it was used in another experiment.

*Experiment 21 (to test presence of infection in young ticks).—* August 29, 1891, a large number of young ticks nearly  $1\frac{1}{2}$  months old, and still confined in the glass dish in which they were hatched, were crushed in a mortar in sterile distilled water. The turbid brownish liquid was filtered through two thicknesses of filter paper. A portion of this filtrate was passed through a Pasteur filter to remove organisms of every kind.

No. 165 (heifer,  $2\frac{1}{2}$  years) received into the right jugular vein 10 cubic centimeters of the fluid passed through the Pasteur filter.

No. 183 (heifer,  $2\frac{1}{2}$  years) received into the right jugular vein 5 cubic centimeters of the turbid fluid not passed through a Pasteur filter. Repeated examination of the blood in both cases failed to show any disease.

In 1892 a similar experiment was tried with equally negative outcome. Nos. 202 and 207 were used for this purpose, and their history, together with the blood examinations, may be found in the appendix.

The result of these two experiments is at present inexplicable. The crushed ticks introduced into the blood fail to produce any infection whatever, while ticks from the same lots when placed on the skin (see No. 224) produce Texas fever. The experiment simply demonstrates our incomplete knowledge of the life history of this parasite.

#### GENERAL SUMMARY OF THE FIELD EXPERIMENTS RELATING TO THE CATTLE TICK .

We are now in a position to review the results of the field work of the past four summers and determine how far they enable us

to draw definite conclusions. In addition to the general control experiments (Experiments No. 1, 3, 4, 8, 9, 14, and 17) by which Texas fever was produced in the natural way in natives which pastured on the same ground with Southern (North Carolina and Texas) cattle, experiments have been carried on in the three directions outlined on p. 92.

(1) Experiments with Southern cattle from which the ticks were picked off were made every year. (Experiments No. 2, 5, 11, 15, 18, and 19.) Those made in 1889 and 1892 were successful. Those made in 1890 and 1891 failed because young ticks appeared subsequently. The conclusion from these experiments that the tick is necessary to cause infection in Northern cattle may be regarded as demonstrated.

(2) Experiments to show that fields may be infected by cattle ticks alone were made in 1889 and 1890. (Experiments No. 6, 10.) In both Texas fever was produced.

(3) Experiments to show that young ticks artificially hatched produce Texas fever when placed on susceptible cattle were made in 1890, 1891, and 1892. (Experiments No. 12, 13, 16.) These were uniformly successful in the summer and fall months.

It was observed, however, that the disease induced by such ticks is less fatal than that produced in the fields in the natural way. We are not prepared to account for this difference, unless it be the mode of incubation. The artificial condition of heat and moisture under which the eggs are kept may lead to a speedy destruction of the microparasites which are in some unknown way associated with them.

(p. 261)

THE RELATION OF THE CATTLE TICK TO THE "PERIOD OF INCUBATION" OF TEXAS FEVER AND TO THE INFECTIOUSNESS OF SOUTHERN CATTLE

In the foregoing experiment everything points to the cattle tick as the natural transmitter of the disease. It has been definitely demonstrated by our experiments that not only fields may be infected by simply scattering matured ticks over them, but that cattle themselves may be infected in stables away from all

infected ground by placing on them young ticks artificially hatched.

We are now in a position to understand the peculiar variability in the period of incubation. We have seen from the experiments related that when native cattle are exposed to Southern cattle on a given field the period elapsing before the disease appears is generally over forty-five days, and the first deaths usually occur one or two weeks later, as is illustrated by the following table:

Year	Experiment	Date of exposure	First high morning temperature	First death	Number of days after exposure
1889	1	June 27.....	Aug. 15.....	Aug. 23.....	57
1890	9	July 4.....	Aug. 18.....	Aug. 27.....	54
1890	8	July 4 and 5...	Aug. 23.....	Aug. 29.....	55
1891	14	July 2.....	Aug. 18.....	Aug. 29.....	58
1892	17	July 1.....	Aug. 16*....	Aug. 22.....	52

\* There was a period of high evening temperature in this field 20-25, the significance of which is not clear.

This long period coincides with the time necessary to produce a new generation of ticks. When Southern cattle graze on a certain pasture in early summer, say for a day only, a few ripe ticks drop off. They lay their eggs in about seven days. These are hatched in about twenty days, and are at once ready to crawl on cattle. Ten days thereafter the first high temperature usually appears. If we add these figures together we find that the disease may appear about thirty-seven days after the field was infected.\* To be sure, these figures are liable to fluctuations which may make this period much longer, or perhaps a little shorter at times.

When Southern cattle are placed on a certain field and kept there, as in our experiments, the field becomes much more abundantly infected with ticks, for the reason that all the ticks in their various stages ripen and fall on the same ground. Hence there is a continuous infection of the field going on for several weeks,

\* In 1890 the Texas-fever parasite was first detected thirty-four days after the first day of field infection.

until all the ticks originally attached to the Southern cattle have disappeared. This may increase the severity of the disease.

But how may we account for the fact that cattle placed on infected pastures later may become diseased at the same time, and may die in less than fifteen days after the first day of exposure? Simply by taking into account the fact that cattle exposed late are at once attacked by the young ticks already present on the field. Hence, if we allow ten days for the fever to appear after the ticks have crawled on the cattle the mystery is at once explained.

The explanation of unusually prolonged periods of incubation is equally simple. They are associated with very early importations of (p. 262) cattle, and the low temperature retards the development of the young in the egg. We have already shown that this development may be greatly retarded by cold, and we have observed periods of incubation ranging from twenty to forty-five days, and have kept eggs over winter which developed when the temperature became warm enough the following spring.

Billings has compiled a table (8, p. 47) embracing ten outbreaks of Texas fever which have occurred in various Western States since 1868. The period elapsing from the date of exposure to that of the first death ranges from thirty-three to ninety days. Leaving out of account these two extreme periods, the remaining ones range between forty-six and sixty-five days. The short period of thirty-three days is probably due to the fact that the native cattle were exposed on a field which had been infected some time before, and on which the tick eggs had consequently undergone more or less development. This is made highly probable by putting this outbreak with the one after it in the table.

(6) Tolono, Ill., June 25, 1868 (date of arrival of Texans). . . . July 28 (first death). Period 33 days.

(7) Sodus, Ill., June 1, 1868 (date of arrival of Texans). . . . July 28 (first death). Period fifty-six days.

Tolono and Sodus are on the same railroad and but 5 miles apart. The Sodus fields were infected June 1, and the period of incubation is fifty-six days, the usual time. The Tolono fields

were most likely infected at the same time, since the first death occurred at both places on the same day. That they were not also infected twenty-five days later we do not pretend to gainsay. At this time of the year, i.e., June and July, the period of thirty-three days is somewhat short for the appearance of a new generation of ticks, and the explanation given will clear up this difficulty. Billings has furnished a very good illustration (8, p. 47) of the prolongation of the period between infection of pastures and the appearance of the disease in an outbreak at Tekamah, Nebr., studied by him in 1887. The Texans infected the field as early as April 1, or thereabout, but the disease did not appear until ninety days thereafter.

There is general unanimity on this point, that a long period elapses between the date of infection of a given pasture and the appearance of the disease, so that further illustrations may be dispensed with. In searching over all the various publications on this subject we have not yet encountered any authentic statement which gave dates to support its claims that Texas fever ever appeared on a field within thirty days of the time that it was entered by tick-bearing cattle. If there are any such outbreaks they may have been produced either by ticks wintering over in the egg, or by an infection of the field earlier than that actually noted. It is not improbable that Southern animals may accidentally carry some eggs of ticks, nearly hatched, on their feet or other parts of their body. In such a case disease might appear several weeks earlier. The same would be true if ticks which have once attached themselves to cattle should, after being accidentally torn or brushed off, crawl upon natives, provided they are still infectious.

The relation of young ticks to Texas fever explains why natives placed in an infected inclosure at various intervals before the appearance of the young ticks will all contract the disease at the same time. They may mingle with freshly arrived Southern stock for twenty or twenty-five days before becoming infected. If removed at the end of this period before the appearance of young ticks they remain healthy. (See Expt. 17.) We now understand why natives placed on an infected field (p. 263)

after the young ticks have appeared will contract Texas fever in ten to fifteen days. The life history of the tick likewise explains the frequently observed fact that Southern cattle lose the power of infecting Northern pastures after a certain number of days. We have already stated that the ticks on Southern cattle gradually disappear as they become matured. It is evident that when all have dropped off the power of the cattle to infect fields is lost. It is possible to give the exact period of time required, provided we know the time which has elapsed since Southern cattle left their pastures, where they are being continually infected with young ticks. On the station pastures the time required for all the ticks to disappear was twenty-five to thirty days. Very soon thereafter the young ticks, descended from the ticks which matured first, appeared on all cattle, and the Southern animals again became infectious. The maturation of the second generation may push the period of disease into the fall and thereby rob it of its fatality.

We now likewise understand how cattle driven slowly northward lose their infection after a time. As soon as they have left the territory where ticks abound they receive no more accessions of young ticks, and they are continually dropping mature ones. After twenty-five to thirty days, or perhaps sooner, they have parted with all and are henceforth harmless to Northern stock.

Let us now review briefly what occurs when Southern tick-bearing cattle are placed in the same inclosure with natives. If the animals be brought together early in July, as in our experiments, nothing unusual will be noticed for weeks. The ticks on the Southern animals slowly mature, swell up, and drop off, one by one, so that after three or four weeks all have practically disappeared. If, during the second week in August, the cattle be carefully examined, young ticks will be found attached to the skin and buried within the coat of hair. They may be overlooked if the examination is superficial and hasty. A week later, generally in the third week in August, the temperatures of all exposed native cattle suddenly rise to  $105^{\circ}$  or  $107^{\circ}\text{F.}$  within a few days of one another. The ticks at this time are still quite

small, and have not yet passed through the second molt. Even at the post-mortem examination of many cases only small, immature ticks are found. If the natives survive the attack, the ticks mature, swell up, and drop off, ready to give birth to a second generation if the season permits.

THE RELATION OF THE CATTLE TICK TO THE MICROÖRGANISM OF  
TEXAS FEVER

The hypothesis which seemed most plausible after the experiments of 1889 was that the tick, while withdrawing the blood from Southern cattle, drew out in it the Texas-fever parasite, which, entering into some more resistant state, perhaps some spore state, was disseminated over the pastures when the body of the mother tick became disintegrated. These spores were then supposed to enter the alimentary tract with the food and infect the body from this direction. The later experiments, however, completely demolished this conception. Neither the feeding of adult ticks and tick eggs nor the feeding of grass from infected pastures gave any positive results. On the other hand, the unmistakable outcome of the experiments was that the young tick introduced the infection into the body. This fact implies two possibilities. Either the tick is a necessary or a merely accidental bearer of the microparasite. If a necessary bearer of the infection, we must assume that the latter undergoes certain migrations and perhaps certain (p. 264) changes of state in the body of the adult tick and finally becomes lodged in the ovum. Subsequently it may become localized in certain glands of the young tick and discharge thence into the blood of cattle. This hypothesis assumes a complex symbiosis between the tick and the parasite on the one hand and the cattle and the tick on the other. According to another simpler hypothesis the tick would be merely an accidental bearer of the infection. The parasite entering the body of the tick with the blood of cattle may be already in the spore state or about to enter upon such a state. The young ticks, as they are hatched near the dead body of the female, may become infected from this. This infection, clinging to their mouth parts, is introduced into the blood of the

cattle to which they subsequently attach themselves. Further investigations are necessary before the probable truth of one or the other of these hypotheses can be predicted with any degree of certainty.

It should be stated that the contents of the bodies of ticks in various stages of growth have been examined microscopically with considerable care. The abundant particles resulting from the breaking up of the ingested blood corpuscles obscured the search so that nothing definite has thus far resulted from it. The very minute size of the microorganism renders its identification well-nigh impossible, and any attempts will be fraught with great difficulties.

A question of much interest, but one upon which we have no information, is the relation of the cattle tick to the enzoötic Texas fever area. Is the distribution of the tick coextensive with that of the Texas fever microparasite, or does their distribution obey different laws? This question could be solved by a thorough investigation of a small portion of the border line of the enzoötic territory. This border line probably depends on the mean annual temperature, and hence we can not expect to find it very sharply defined. Ticks may extend farther north during some seasons than others, and hence there may be a belt or strip on which cattle are partially insusceptible because of former repeated attacks, although for the time being ticks may be absent. The entire subject is at present speculative, and is simply referred to here to arouse the attention of those who are in a position to record observations concerning it.

#### THE RELATION OF SOUTHERN CATTLE TO THE TEXAS-FEVER INFECTION

What has already been said concerning the tick makes it certain that all Southern cattle are dangerous when they bear the cattle tick, whether they are sick or healthy. On the experiment station fields, the North Carolina and Texan cattle which called forth Texas fever during the four years of the investigation were, in general, healthy. Two cows were killed. One of these had impoverished blood, although positive signs of Texas



fever were not detected. Another died of peritonitis. The remainder were healthy, improved on the pastures, and were sold at the beginning of winter or before.

In the foregoing pages it has been assumed that the tick obtains the microparasite from Southern cattle. Without demonstration it might be claimed with equal propriety that the microparasite belongs essentially to the cattle tick, and that its multiplication in the body of susceptible cattle is perhaps an accidental phenomenon against which Southern cattle have been amply protected by frequent infection. Experiments made latterly, as well as the microscopic examination of the (p. 265) blood, prove that the microparasite is harbored by Southern cattle in a state of health. These interesting experiments, as far as they have been carried up to the present, are briefly summarized here. The complete record of these cases will be found on page 298.

*Inoculation with blood of healthy North Carolina cows soon after the latter had left the Southern pasture.*—On July 6, 1892, a native cow, No. 198, received into a jugular vein 28 cc. of blood drawn from a jugular vein of a North Carolina cow, No. 217. The quantity of blood injected was large, because it was supposed that if the microorganisms were present at all in the Southern cattle, they would be very scarce. The blood was drawn from the Southern cow by piercing the wall of the vein with the needle of a previously sterilized and warmed hypodermic syringe, holding 14 cc., and injected immediately after into the exposed jugular of the native cow by simply piercing the wall of the vein. The entire operation lasted about two minutes. The high temperature became continuous on the seventh day after inoculation, and the number of red blood corpuscles had begun to fall on this same day. The various symptoms of Texas fever became gradually intensified, and the animal died July 19, thirteen days after inoculation. On the day before death the urine was claret-colored. The autopsy revealed the usual lesions of Texas fever.

On the same day No. 206, another native cow, was inoculated in the same way with blood drawn from a jugular vein of North Carolina cow, No. 216. The same quantity, 28 cc., was injected as before, 14 cc. being injected at a time. The high temperature

and the destruction of red blood corpuscles set in at the same time with those of the preceding case. This animal did not die, however. After passing through a prolonged fever period the animal slowly recovered to suffer a relapse, which kept the number of red corpuscles below 2,000,000 during the whole of September.

On July 16, ten days after the preceding inoculations, a third cow, No. 219, received the same quantity of blood into a jugular vein. The blood was drawn from North Carolina cow No. 216. The continuous high temperature began July 24, at which date the destruction of corpuscles had set in. The further history of this case is very similar to that of the preceding, No. 206. The blood corpuscles continued to decrease in number until August 6. After this there was a slow rise. At the end of August a relapse was detected, which continued throughout September.

*Inoculation with blood of healthy North Carolina cattle sometime after the latter had left the Southern pasture.*—On August 15, a steer, No. 222, received 28 cc. of blood drawn from North Carolina cow No. 214. The same procedure as above was adopted. The disease had become established by August 25, as is shown by the high temperature and the marked reduction in the number of red corpuscles on this day. The movement of the disease was markedly slower so far as this latter phenomenon is concerned. In the middle of September a relapse was detected, which was still in progress at the beginning of the second week in October.

On September 9, a cow, No. 230, received the same quantity of blood from No. 214 into a jugular vein. In this case the first high temperature appeared September 14, and by October 1 the number of red corpuscles had fallen to 2,200,000.

These positive results demonstrate that the Texas fever micro-organism was present in the blood of North Carolina cattle as long as seventy-four days after they had left the permanently infected territory. One cow, No. 217, was tested once on the ninth day; another, No. 216, was (p. 266) tested on the ninth and the twentieth day; a third was tested on the forty-ninth and the seventy-fourth day. That the microörganism was the one found in natives infected in the ordinary way on pastures was

demonstrated in every one of the five cases by a large number of microscopic examinations. No difference whatever could be detected. Moreover, three out of the five inoculated cases passed through relapses or mild secondary attacks, in which the stage of the peripheral coccus-like body appeared constantly in the blood, as in the ordinary mild type of the disease. There can be no doubt, therefore, that the microparasite transmitted in the blood of Southern cattle was the same as the one introduced into the blood of natives by the cattle tick.

It might be claimed the Southern cattle harbored this microparasite because they are being constantly reinfected by the cattle tick. This might be true of Nos. 216 and 217, but it does not hold for No. 214. This animal was one of the four from which the ticks had been carefully picked in July, so that at the date of the last inoculation with blood from this animal it must have been entirely free from ticks for at least fifty days, and it had received no fresh accession of ticks since leaving its native pasture, June 27 (seventy-four days).

Whether the Texas fever parasite resides permanently in the bodies of Southern cattle or whether its presence, after all, depends on that of the cattle tick, these experiments do not permit us to decide definitely at present.\* From an economic standpoint this is of little importance, since in many parts of the permanently infected territory of the South ticks are present during the entire year.

The presence of the parasite in Southern cattle does not seem to materially affect their health, although it may maintain a more or less constant breaking up of the red corpuscles on a small scale, which would necessarily tax certain vital organs. The parasite is present in the circulating blood in such small numbers,

\* The production of disease in 1891, by ticks which wintered over on one of the fields of the station, would at first sight suggest the inference that the cattle tick carried the parasite through the winter in the egg. This does not follow from the circumstances, however, for there were in the same inclosure Southern cattle which had been kept over one or two years for purposes of reëxposure. Ticks hatched in spring may have invaded all the cattle in the inclosure, matured and dropped off, and given rise to another generation, which produced the disease late in August. This second generation may have obtained the microparasite from the Southern cattle.

however, that only after a most tedious microscopic examination is it occasionally encountered. The fact that Southern cattle rid themselves of infectious properties on Northern pastures after twenty-five to thirty days does not, therefore, imply that their blood is no longer infectious. It simply signifies that they have rid themselves of the means by which this parasite is transmitted, namely, the cattle tick.

In the various Southern animals whose blood was examined at one time or another during these investigations, the number of red blood corpuscles was, in general, fully up to the level maintained by the natives used in the experiments. A few Southern animals were kept on the station grounds for longer periods, and subsequently exposed to Texas fever infection fresh from the South. Of these, No. 117 exposed, in winter, five months after arrival from the South, Nos. 32, 62, and 59 exposed one year thereafter, and Nos. 55 and 60 two years thereafter, showed the normal number of red corpuscles.

The discussion which has raged so persistently about the health of Southern cattle has outlived its usefulness or suggestiveness, for it does not matter in what condition they are. So far as our evidence (p. 267) goes—and this is very strong—they are quite harmless, provided they do not carry the cattle tick. Hence there is no necessity for going into a review of the statements of Gamgee, the Metropolitan Board, and of F. S. Billings on this point. It is not claimed that Southern cattle may not and do not contract Texas fever. It is highly probable that every Southern calf has to go through the process of natural inoculation and reinoculation to a greater or less extent, and we have the records of several calves of Southern parents which passed through a mild form of the disease. It is likewise probable that a certain percentage of Southern animals which have not been sufficiently exposed while young may contract Texas fever in adult life under abnormal conditions. It is not impossible that under the influence of prolonged marches, crowding in cattle cars and on vessels, with insufficient air and food, the natural resistance of the body may break down and the mild or unobserved infection break out into an acute disease. These are

possibilities as yet unproved, but they are by no means ignored when we state that Southern cattle, to all appearances healthy, do transmit Texas fever, and it is not necessary that they have any symptoms of disease, recognizable by clinical methods, to make them dangerous. We do not now wish to enter into philosophical discussion as to what constitutes disease. From a practical economic standpoint we must maintain that Southern cattle may be healthy and yet be the cause of Texas fever.

The various hypotheses which observers have framed concerning the infectious character of the excreta of cattle, the saliva hypothesis of Detmers, the manure hypothesis of Billings, or the urine hypothesis of others must now be considered as unfounded so far as these excreta are claimed to be the direct source of the disease, since the excreta of Southern cattle on Northern fields can not produce Texas fever. In those experiments which demonstrate that Southern cattle may pasture with susceptible Northern cattle throughout the summer without imparting disease, provided all ticks be removed, we have all the necessary proof for refuting these hypotheses, since the excreta and the secretions of all kinds are left on the field. The only object missing is the cattle tick.

#### SICK NATIVES AS SOURCES OF INFECTION WHEN THE CATTLE TICK IS PRESENT

This matter has called forth much discussion by scientific observers as well as by cattle-owners. It is a question of considerable importance to determine whether cattle which have contracted Texas fever in the ordinary way may transmit it to other natives coming in contact with them. That such transmission must be very rare is evident, otherwise there would have been no discussion and no divergent opinions. It is certainly a very curious fact that animals, which are affected with an infectious disease contracted indirectly through the presence of certain presumably healthy cattle, should not also transmit the same disease to other susceptible cattle. Theoretically, there is nothing opposed to the view that sick natives may infect other natives, and we shall show that they actually do so; but the

conditions under which this infection takes place are rarely realized, and hence very little disease due to natives comes under observation. The fact that the disease may be transmitted from sick to healthy natives directly by injections of blood into the veins does not help us in solving the problem before us, since the disease is not conveyed in this way. If we turn, however, to the life history of the tick we shall find the explanation sought.

Sick natives have ticks on them. But only those which survive the (p. 268) disease or die after a prolonged attack ripen the tick on their bodies. Those which die of an acute attack in a short time after infection have only immature ticks on them. If the fever has occurred early enough in the season to permit a second generation of ticks to appear before the cold weather arrives, we may expect Texas fever on fields on which sick natives only have pastured. Usually the first outbreak occurs in August, and the second, to be looked for in late September or early October, is so mild as to pass unobserved. If, however, the first outbreak occurs in July, the second may appear in September and perhaps be of greater virulence.

In order to test this problem the following experiment was carried out:

In 1890 Field IV (see Fig. 5, p. 248) was set aside to be infected with sick natives only. The following sick animals were introduced:

August 21.—No. 49 and calf No. 85, exposed in Field VI since July 4; elevated temperature since August 19.

August 21.—No. 105, exposed in Field VIII (ticks only) July 4; elevated temperature since August 13.

September 3.—No. 50, exposed in Field VI July 4; elevated temperature since August 27.

September 5.—No. 47, exposed in Field VIII (ticks only) August 21; elevated temperature since September 1.

September 8.—No. 135, exposed in Field VIII (ticks only) August 21; elevated temperature since August 30.

All these cases, excepting the calf, went through a severe attack of Texas fever, to which No. 47 and No. 50 succumbed.

The field was therefore infected, so far as this was possible, by sick natives.

In this field were placed two natives (Nos. 132, 133) on August 21. These animals passed through a mild but undoubted attack of Texas fever. In both blood parasites were observed early in October, and the number of red corpuscles shows evidence of infection after the middle of September. Though this experiment is sufficient to demonstrate the ability of sick natives to infect pastures, a much more obvious and striking result might be obtained by an early infection of the fields.\*

There are several instances reported of the transmission of disease by sick natives. The Metropolitan Board of New York City reported an outbreak of Texas fever among cattle at Hamptonburg, Orange County, N. Y. (1, p. 954), due to the importation of native cows from Painesville, Ohio, on the Lake Shore Railroad, over which a large number of Texas cattle had been passing. The disease, supposed to have been introduced by the Ohio natives, broke out in October, 1868, and deaths occurred as late as October 24 and 27. The cows brought from Ohio were received August 25, and deaths occurred among them on that day and up to September 10. It is also stated that several native cows died of Texas fever, fourteen, sixteen, and nineteen days after exposure to these infected natives. This last statement is open to question, for if our deductions be correct and the general experience of those who have observed Texas fever be trustworthy, it would take from one and a half to two months for such infection to take place.

A very good illustration of the infecting power of diseased natives is that given by F. S. Billings (8, p. 41). According to his statement 1,100 Texan cattle reached Tekamah, Nebr., March 30-31, 1887. Twenty-one native cows put into one of the infected pastures May 1 began to die early in July. On June 19, twenty-four native steers (p. 269) broke into a pasture infected April 1-15 by the Texan cattle. They were returned next day to a pasture containing 114 natives. The twenty-four steers

\* A similar experiment in the artificially heated stable with the progeny of ticks matured on sick natives is not conclusive on this point.

began to show signs of disease July 9, and only two recovered. Curiously enough, Texas fever broke out among the 114 natives, and several were found dead September 21. These circumstances are all perfectly intelligible, if we apply the facts which we have worked out concerning the life-history of the cattle tick and its relation to Texas fever. It is to be regretted that Billings did not make any observations on the ticks present on the infected cattle.

We will take it for granted that the Texan cattle brought cattle ticks with them, and that ripe females dropped on the pastures about Tekamah, Nebr., from April 1 to April 15. We have received such from North Carolina in midwinter, which, confined in a paper box in the laboratory, promptly laid a large number of eggs. It might be claimed that at this date the low temperature would destroy the ticks entirely. It is true that low temperatures interfere with the growth of ticks on cattle and with the development of the young tick in the egg, but the embryo is not destroyed, but simply lies dormant until the warming season approaches. Thus, the experiment station ticks (probably in the egg), actually wintered over on a wooded pasture in 1890-'91. We are indebted to the Weather Bureau for the daily maximum and minimum temperature of De Soto, Nebr., about 25 miles south of Tekamah, from March 30 to May 15, 1887. From this table we learn that the thermometer fell at night below 32°F. only seven times after March 30, and that on April 8 the maximum temperature was 92°F. There was nothing in the weather, therefore, to prevent the ripe ticks laying their eggs. The young ticks probably did not hatch before the middle of June, because the 21 native cows which were put on an infected pasture did not begin to die until early in July. The 24 steers which broke into an infected pasture June 19 began to show signs of disease at about the same time (July 9). This short period of twenty days indicates that the ticks were probably just hatched when these steers broke in.

The time of infection of the large lot of natives by these steers may be easily calculated. They returned from the infected pastures June 20 with young ticks on them. If we allow twenty to



twenty-five days for maturing, seven to ten days for egg-laying, twenty days for hatching, ten to fifteen days for the appearance of the fever, and seven to fourteen days for the first fatal case, we have in all sixty-four to eighty-four days from June 20 for the first death among the natives infected by natives. This would bring us to August 23 or September 12 as the probable date of the appearance of the disease originating from ticks which matured on native cattle. The actual date was September 21. Or we may calculate it in another way. When Southern cattle infect the ground by simply passing over it, they do so by dropping ripe ticks ready to lay their eggs. In such a case we usually find a period of fifty-five to sixty days elapses before the first death. In the case before us the 24 steers which broke into the infected pasture June 19 brought only young ticks with them. Hence, to the usual period of fifty-five to sixty days, we must add twenty to twenty-five days to allow the ticks on the natives steers to ripen. This would make the period seventy-five to eighty-five days, and the first death might occur between September 3 and September 13, provided the case were acute and rapidly fatal, as is the case in midsummer.

The mortality of such secondary outbreaks due to sick natives is probably very low. In the case before us we are not told definitely by (p. 270) Billings how many of the 114 head exposed to sick natives succumbed, excepting that several were dead on a certain date. It has already been stated that only those natives which survive, or die after prolonged illness, can mature ticks on their bodies. Hence, where the mortality is very high, the ticks may mature in but small numbers, so that the secondary outbreak due to sick natives may be mild for this reason as well as on account of the advanced season; for there seems to be, up to a certain point, a more or less direct relation between the number of ticks which attack cattle and the severity of the disease.

In regard to the infectious character of sick natives it may be concluded that the infection really exists, and it may be transmitted to other natives by the cattle tick. The severity of the secondary disease will depend upon the time of the first outbreak among the natives and upon the number of ticks matured. It

is as a whole not a very serious element, and the losses result mainly from the impoverished condition of the animals which pass through such attacks.

SICK NATIVES ARE HARMLESS WHEN THE CATTLE TICK IS  
ABSENT

This investigation is largely of theoretical interest in confirming the experiments which demonstrate that Texas fever is not transmitted from Southern to Northern stock without the intermediation of the cattle tick. Natives are not supposed to be sick excepting as they are infected by the cattle tick, hence the existence of sick natives without ticks must be of such rare occurrence that it is of no practical importance. In the following experiment the disease was produced in native cattle by the intravenous injection of blood drawn from the jugular vein of healthy Southern cattle. For a more complete discussion of these inoculations, the reader is referred to page 265, and to the history of the individual cases given elsewhere. Here we simply mention the fact that the disease was actually produced, and that two natives, placed with such cases as controls, remained well, as is indicated in the annexed table:

Date	No.	Quantity of blood injected into vein	Source of blood	Remarks
1892				
July 6	198	28 cc....	N. C. cow, 217....	Disease begins July 13. Cow dead July 19.
July 6	206	28 cc....	N. C. cow, 216....	Disease begins July 13. Acute attack followed by relapse in September. Recovery.
July 16	219	28 cc....	N. C. cow, 216....	Disease begins July 13. Acute attack followed by relapse in September. Recovery.
Aug. 15	222	28 cc....	N. C. cow, 214....	Disease begins August 18. Recovery.
Sept. 9	230	28 cc....	N. C. cow, 214....	Disease begins September 14. Recovery.
July 16	218			October 1, exposure negative.
Aug. 15	221			October 1, exposure negative.

The disease began in this field as early as July 13. Five animals had passed through the disease and one had died on it. The control, No. 218, had been in it from July 16, i.e., seventy-seven days up to October 1 without manifesting the slightest signs of infection. The second control spent forty-six days in this inclosure up to October 1, with the same negative outcome.

(p. 271) MAY TEXAS FEVER BE COMMUNICATED BY AGENCIES  
OTHER THAN THE CATTLE TICK?

We have seen in the foregoing pages that the transmission of Texas cattle fever may be prevented entirely by removing the ticks from Southern cattle in such a way that a new generation is suppressed. We have likewise seen that sick natives may remain in the same inclosure with healthy natives for months without transmitting the disease to them, provided the sick natives have no ticks on them, or, in other words provided the disease has been produced by direct inoculation. These facts go far toward bringing us to the conclusion that no outbreaks of Texas fever are produced without ticks. Yet we can not deny the possibility of a conveyance of the disease by other agencies, for this possibility is demonstrated by the fact that by a direct transference of blood from sick natives, and even from healthy Southern animals, the disease may be reproduced with all its characteristic virulence. We know as yet so little of the ectogenic life of the Texas-fever parasite that whatever hypothesis may be made must remain such until our knowledge has become more defined. Meanwhile we may formulate certain possibilities of transmission without the aid of the cattle tick to call the attention of future observers to them.

It is possible that the disease may be conveyed by insects, which pierce the skin and draw blood. Such pests, when moving from sick to healthy animals very rapidly, may carry enough blood on their mouth parts to inoculate healthy animals. But under such circumstances several factors come into play, such as the probable destruction of the microparasite by drying and other unknown agencies, and the probability that the quantity of blood is too small to contain any parasites. Moreover, a

single parasite, or even a few parasites, may not produce anything more than a mild, unnoticed affection. The possibility of direct inoculation by insects may depend on the distribution of insects which draw blood. In the District of Columbia Texas fever was not carried by insects, with the possible exception of a single instance, to be described below, during the four summers of work from 1889 to 1892, inclusive, although the very best opportunities were offered them to carry on direct inoculation, especially during the present summer. There may be parts of our country, however, where such direct inoculation from sick to healthy natives in midsummer is favored by the presence of certain insects not to be found near Washington.

If we consider for a moment the probability of an infection of native from Southern cattle directly by means of flies, etc., we shall find it very slight. Though we now know that Texas fever parasites exist in the blood of presumably healthy Southern animals, we must regard these parasites so scarce in number, if we are to be guided by the microscopic examinations of the blood, that insects can not draw enough blood to become dangerous. The infection of natives by Southern animals in this way must be considered probable only when authentic cases of this disease are on record which appeared ten or fifteen days after contact with Southern cattle, *provided the ground has not been previously infected with ticks from other Southern herds*. There seems to be no carefully investigated outbreak of Texas fever on record which occurred within thirty days of the ground infection or of contact with Southern animals.

In case Southern droves of cattle contain animals actually diseased with Texas fever, their blood would contain more parasites than that (p. 272) of the healthy, and hence might serve more readily as an inoculating fluid for insects, but Southern animals and natives are not allowed to mingle so as to bring this about. The disease is produced, in most cases, where Southern and native cattle do not come in contact at all. If insects distribute Texas fever they could only do it accidentally, and hence the result would be a few isolated cases. But Texas fever attacks 90 to 95 per cent of all natives.

Texas fever, as elucidated in the foregoing pages, is essentially a disease of the blood. The parasite producing it must be transferred in some manner from the blood of one animal to that of another. There is no evidence to support the view that it may gain entrance by way of the digestive tract, and hence several channels by which the microparasite might get into the body are necessarily cut off. Though the parasite is very likely present in the discharges and the urine of the sick, and perhaps in smaller numbers in the excretions of Southern animals, yet pastures infected by such excretions are not infectious. In 1890 the following experiment was made:

Blood and spleen pulp from several natives which had succumbed to Texas fever were scattered over the ground in inclosure V, and two natives pastured in it from August 25 to November. There was no trace of Texas fever discovered in either case, although the blood was examined at three different times. The number of blood corpuscles in one of these animals was below normal, but as it remained at this low point throughout the season, and as the animal had some vaginal discharge, the low number must have been due to disturbances of the generative organs. In the other animal the red corpuscles remained above 5,700,000.

Perhaps the best evidence which can be adduced that the excretions do not have anything to do in transmitting the disease is the experiment in which healthy natives are exposed to sick natives free from ticks for months without any result.

The only exception, and this a doubtful one, to the general result of our experiments and experiences at the station, that Texas fever appears only with ticks on native cattle, occurred in 1891. Field XII (see Fig. 7, p. 256) was used only for the storing of unused healthy cattle during the course of the experiments of that summer. In this field a cow was kept (No. 168) upon which bleeding had been performed a number of times for the study of changes going on in the blood in anaemic conditions. The examination of the blood in this case began August 3 and was continued at intervals to September 8. The animal was led

out of the field during each examination to a box, into which she was fastened during the venesection and the collection of the blood. On September 1 No. 162 was received and placed in this field. On September 26 she was observed to be dull and to refuse to eat. The temperature on September 28 was over  $104^{\circ}\text{F}$ . On the following day the animal was found dead. The autopsy revealed an acute case of Texas fever with an enormous infection of the red corpuscles of the blood with the Texas-fever parasite. An examination of the other animals in this field showed that only one other was diseased. This was the case upon which venesection had been practiced, and whose blood had been examined last on September 8. How was this infection brought about? In a preliminary report\* the probability of direct inoculation by flies was emphasized. The disease had appeared on the station as early as August 8 in those cases artificially infected with young ticks, and it appeared (p. 273) subsequently in the general control field VI. Hence the opportunity was afforded for the conveyance of the virus by insects from sick animals. Instead of this channel of infection there is one other possible one. Though no ticks could be found on the animals in this field, a few may have been carried there in the course of the season, or they may have crawled there. A few ticks on an animal may have been overlooked, since they are still quite small when animals succumb in the acute stage. Moreover they may have attached themselves in places not regularly selected by the young ticks (inner aspect of thighs and escutcheon), in which case they would have been quite certainly overlooked. On the whole we must confess that the infection of these two animals is a matter the obscurity of which can not be cleared up. They are the only cases of Texas fever which have occurred on the station fields during the four summers of experimentation which are not directly traceable to Southern cattle carrying ticks, to ticks alone, or to direct transference of blood from sick native or healthy Southern animals to susceptible natives by inoculation.

\* Report of the Secretary of Agriculture for 1891, p. 134.

## IMMUNITY AND PROTECTIVE INOCULATION—DISTRIBUTION OF DISEASES RESEMBLING TEXAS FEVER ON OTHER CONTINENTS

*Immunity in Southern cattle*

It has been stated by some observers that Southern cattle soon lose their immunity against Texas fever after they have been taken to Northern pastures, and that they are liable to be attacked by this disease after having been away from the permanently infected territory for a year or longer. These statements, so far as we know, are not based upon experimental evidence, but upon observation of natural outbreaks, and hence the evidence is likely to be weak in one or more points. As we were more or less favorably situated to test these statements, some of the Southern animals were kept on the station grounds for one or two winters and then reëxposed to freshly imported Southern animals, together with Northern stock. These experiments are a part of those already described in connection with ticks, and the following numbers, therefore, belong to the original experiments.

*Experiment 8 (exposure of native to Texan cattle).*—In addition to the natives, a Southern animal (No. 62), brought from North Carolina in 1889, was exposed on this field September 25, 1890, with a native (No. 74). The latter died October 16, while the Southern animal appeared not to be affected. The blood was examined three times. The corpuscles did not fall below five and one-half millions. All adult natives exposed in this inclosure during the summer succumbed to Texas fever.

*Experiment 9 (exposure of natives to North Carolina cattle).*—In addition to the natives placed in this inclosure, the following North Carolina cattle of the previous year were introduced July 4, 1890:

- No. 32 (heifer, 3 years). Exposure negative.
- No. 59 (cow, 5 years). Exposure negative.
- No. 87 (calf of No. 59, 3½ months). Slight infection.
- No. 61 (steer, 2 years). Exposure negative.
- No. 67 (cow, 5 years). Exposure negative.
- No. 86 (calf of No. 67, 2 months). Slight infection.

From this table it will be seen in the first place that none of the cattle died or became visibly diseased. In Nos. 32 and 59 the blood was examined September 3, when all exposed natives were either sick or dead, and found normal. Nos. 61 and 67 were not examined in this (p. 274) way. In case of the two Southern calves descended from Southern parents, but born on the station, there was a slight infection characterized by the presence of the intraglobular coccus-like stage of the Texas-fever parasite. In No. 87 these were detected September 20, but the blood corpuscles did not fall below five millions, as far as the few examinations are evidence. In No. 86, the younger calf, there was a decided fall in the number of red corpuscles associated with the presence of the parasite in the same stage as in No. 87. The corpuscles numbered but three and one-half millions October 30.

*Experiment 14 (exposure of natives to North Carolina cattle).*—In addition to the natives placed in this field the following Southern animals were introduced July 2, 1891:

No. 55 (cow, 5 years old, from North Carolina in 1889). Exposure negative.

No. 62 (heifer, 3 years old, from North Carolina in 1889, exposed in 1890). Exposure negative.

No. 121 (cow, 4 years old, from Texas in 1890). Exposure negative.

No. 126 (cow, 6 years old, from Texas in 1890). Exposure negative.

These four exposures proved negative (so far as any outward signs of disease are concerned). No. 55 had been away from Southern pastures and not reëxposed for two years. Her blood August 29 was normal. The blood of Nos. 62, 121, and 126 was not examined. In these experiments the examination of the blood was not carried on systematically, and hence no very definite conclusions can be drawn as to the presence or absence of all disease. However, the examination of the blood of adults when made was negative. It is evident that the immunity of Southern cattle is not lost in one year or in two years. And by this we mean insusceptibility so far as a severe attack is con-



cerned, for none of the adults showed any signs of disease, while none of the exposed natives resisted.

It is especially interesting to note that the two Southern calves exposed for the first time were not entirely insusceptible. A mild form of the disease was detected late in the season, and it is not beyond probability to assume that they may have been slightly affected through the entire summer. This seems to make it probable that Southern animals acquire at least some of their immunity by mild attacks very early in life.

*Natural immunity of Northern cattle*

*Natural immunity of cattle more than 1 year old.*—This we know is very slight, for the mortality in many outbreaks has been found to be nearly 100 per cent. Still, there are animals which have more or less immunity, though never exposed to the virus of this disease. By compiling the cases exposed on the station in the ordinary way to Southern cattle in 1889, 1890, and 1891 (experiments 1, 9, and 14), and rejecting all those exposed after September 15, we may obtain approximate percentage of insusceptible cattle. There were exposed in all during these three years 24 head over 1 year old. Of these only one animal remained unaffected, though exposed twice. This was an old cow (No. 57). The remainder passed through more or less severe attacks and five (Nos. 49, 53, 56, 104, and 159) recovered. Some animals, it is true, were killed, but in a dying condition, and these are included with those that died. It may be said, therefore, that about 95 per cent of adult Northern animals are susceptible to Texas fever. When we examine the record of the animals under 1 year of age we obtain a somewhat different result.

These were exposed in the general fields in 1889 and 1890 in all eight calves. Of these two died in 1889 from an acute attack of Texas fever, (p. 275) and two recovered. The remaining four exposed in 1890 were all affected, but none died of an acute attack. The disease was of the more or less mild, prolonged type, with the intraglobular coccus-like stage of the parasite in the blood.\*

\* It is probable that in all these cases a short acute attack preceded the mild attack.

Some succumbed at the beginning of winter from exhaustion, but not so far as could be discovered from the after effects of Texas fever. In general, calves are not insusceptible to Texas fever, but the disease is milder and the mortality is lower than with those more than 1 year old. Attention is here called to the case of a calf which was found dead thirteen days after birth in a field infected with ticks only (experiment 10). The lesions were unmistakably those of Texas fever.

*Acquired immunity of Northern cattle*

This is a problem of far more economic importance than those just discussed, since it affords us some insight into the possibility of producing immunity artificially. The various field experiments of 1889, 1890, and 1891, furnished a number of animals, some of which had passed through a mild attack, others through an acute attack. Many of these were reëxposed the following year to freshly introduced North Carolina cattle in company with fresh native animals. The following summary includes all such exposures. The number of the experiment corresponds in every case to that already described, of which the one under consideration forms a part.

*Experiment 9.*—The following recovered cases of 1889 were exposed with fresh natives to North Carolina cattle:

July 4, 1890.—No. 51 (cow, 4 years) passed through a mild attack in the fall of 1889.

July 4, 1890.—No. 53 (cow, 2½ years) passed through a fairly severe attack in the fall of 1889.

July 4, 1890.—No. 64 (steer, 3 years) passed through a mild attack in the fall of 1889.

September 20, 1890.—No. 65 (cow, 3½ years) passed through a mild attack in the fall of 1889.

July 4, 1890.—No. 75 (heifer, 16 months) passed through a prolonged attack in the summer of 1889.

In these animals the severity of the first attack is best measured by the intensity of the destruction of red corpuscles. The number of corpuscles in No. 51 had fallen below 1,500,000 on November 4, 1889. In No. 53 they fell to 2,500,000. In No.

64 they had fallen to 2,700,000 on November 7, but there were still many infected corpuscles in the circulation. In No. 65, they numbered only 1,700,000 November 4. No. 75 was not examined. The result of the second exposure in 1890 is, briefly, as follows:

No. 51 dies of an acute attack August 26.

No. 53 probably not affected.

No. 64 passes through a prolonged, but rather mild attack.

No. 65 passes through a mild attack (exposure late) and dies some time after.

No. 75 probably not affected.

*Experiment 10.*—No. 47 (cow,  $4\frac{1}{2}$  years) had passed through a rather severe attack in the fall of 1889. The red corpuscles at that time fell below 1,000,000. July 4, 1890, she was placed in Field VIII, into which only adult cattle ticks had been thrown. She died of an acute attack September 12.

(p. 276) *Experiment 14.*—The following recovered cases of 1890 were exposed with fresh natives to North Carolina cattle July 2, 1891:

No. 56 (steer, 4 years) passed through a prolonged attack in fall of 1890.

No. 102 (cow, 7 years) passed through an acute attack (due to ticks only) in summer of 1890.

No. 130 (cow, 6 years) passed through a rather severe attack (*Experiment 13*) in artificially heated stable (1890-'91).

No. 143 (heifer,  $2\frac{1}{2}$  years) passed through a doubtful attack (*Experiment 13*) in artificially heated stable (1890-'91).

The result of this exposure is, in brief, as follows:

No. 56 passed through a mild attack.

No. 102 was slightly, if at all, affected.

No. 130 died from an acute attack August 27.

No. 143 passed through an acute attack and recovered.

*Experiment 17.*—In addition to the natives, not hitherto exposed, which were placed into Inclosure VI, in 1892, together

with fresh North Carolina cattle and ticks, the following recovered cases were included:

No. 135 reëxposed July 20. This animal had passed through an attack in Field VIII (Ticks only) in 1890. This summer it was again attacked, and the red corpuscles at one time were found as low as 2,000,000.

No. 167 was reëxposed on the same day with the preceding. It had passed through an acute attack last year, and was very low for a time. This summer there was probably a slight attack, as the blood corpuscles, though they did not fall below 5,000,000 showed signs of regeneration.

The following cases were reëxposed together on August 26 in the same field, and a hitherto unexposed native, a bull (No. 204), 2½ years old, was put in with them as a control, since the season was now somewhat advanced:

No. 56 had passed through a prolonged but mild attack in the fall of 1890. In 1891 it was again exposed and passed through a short acute attack. This summer there was probably a very short attack, as is indicated by the record of the red corpuscles.

No. 105 had passed through an acute and prolonged fever in Field VIII (ticks only) in 1890, followed by a relapse later on in the same season. A second exposure in September of 1891 was apparently negative. This summer, however, the disease reappeared on exposure, the loss of red corpuscles being fairly severe.

No. 160 was exposed late in 1891 and passed through a short but acute attack, followed by a relapse which lasted into December. This summer the exposure was evidently negative.

No. 166 was infected with artificially hatched ticks in 1891, and passed through an acute and rather prolonged attack. This summer the exposure was negative.

No. 182 passed through an acute attack late last year as the result of the intravenous injection of infected blood. This year the exposure resulted in a slight attack.

No. 185 at the same time passed through a similar attack, due to inoculation. This summer the exposure was negative.

No. 204. The control exposed at the same time in this field passed through a very acute attack, and was probably saved by its age. No. 225, which had just passed through the disease due to an infection with

artificially hatched ticks, and whose blood corpuscles had nearly reached the normal, was transferred to this field August 30, four days later than the preceding lot. A second attack was the result, with a rapid and extensive loss of corpuscles. This case is merely introduced to show the intensity of the infection still existing in this field, but it can not be wholly regarded in the light of a control.

(p. 277) The following table gives a brief résumé of these exposures:

Nature of attack			
No.	1890	1891	1892
56.....	Mild, prolonged.....	Short, acute.....	Slight (?).
105.....	Acute, prolonged, with relapse.....	Negative.....	Fairly severe.
135.....	Acute.....	.....	Do.
160.....	.....	Short, acute, with relapse	Negative.
166.....	.....	Acute, prolonged.....	Do.
167.....	.....	Acute.....	Slight (?).
182.....	.....	...do.....	Mild, short.
185.....	.....	...do.....	Negative.
204.....	.....	.....	Very acute.
(Control)			

These experiments demonstrate the important fact that one attack of Texas fever does not necessarily protect the animal from a second attack. Of the eighteen cases, seven may be said to have remained practically unaffected during the second exposure. Of the remaining eleven three died during the second exposure. It is impossible to determine in such cases how much natural immunity existed before the first attack. Thus No. 53 survived the first attack, while another cow exposed at the same time and nearly of the same age succumbed to an acute attack. No. 75, the heifer which passed through the first exposure, as a calf 4 months old, is hardly to be regarded as a fair case. Hence we must be cautious in giving even in these cases too much credit to the first attack in warding off the following one. It is not to be denied that in the case of animals not more than  $2\frac{1}{2}$  or 3 years old a first mild acute attack may be followed by a very

mild infection, but it may be laid down as a general proposition that a single attack is not sufficient to produce complete immunity.

*Problems concerning preventive inoculation*

If a single attack of the disease itself does not afford complete protection it is not likely that any process or method of artificial inoculation will be successful in this respect. The profound effect which is necessarily produced in the body of an animal by a destruction of red corpuscles equal in amount to all those circulating in the body at any given time should make much more impression than any other method of inoculation is likely to do. And yet such an attack not only does not prevent a second attack but may not prevent death during a second attack. Aside from the difficulties attending the production of insusceptibility under any circumstances the difficulties of preparing a "vaccine" according to the method hitherto practiced are at present insurmountable. The microörganism which we have described as the presumable cause can not be cultivated. Hence the method first practiced by Pasteur of using an attenuated form of the virus itself is not within reach, and other means must be sought. Before suggesting any lines of experimentation in this field let us examine briefly under what conditions it is desirable to have an animal insusceptible to Texas fever.

On pastures north of the permanently infected area Texas fever can be kept away by properly applied preventive measures. Hence the protection of Northern cattle by some artificial process is unnecessary and practically out of the question. It is, however, of great importance to be able to protect from a fatal attack valuable animals which are to (p. 278) be taken South into permanently infected territories. It is probable that if calves be taken they may, without treatment of any kind, survive the infection upon Southern pastures and become gradually insusceptible. But in case of animals more than 12 to 18 months old the first attack might be fatal, and if a preliminary mild attack could be induced by artificial means the fatal effect of a second attack might be averted.

Perhaps the simplest manner of producing a mild, usually nonfatal attack, is to expose cattle on pastures which have been infected with ripe, egg-laying ticks at some specified time in the fall. This time must depend on the climate of the locality where the infection is to be practiced. In the latitude of Washington we found, in 1889, the middle of September a convenient time for the infection. In more northerly latitudes the exposure should be correspondingly earlier. Cattle exposed in this way take Texas fever invariably, but the mortality is practically zero. Such animals may die of a second attack during the succeeding summer, but a second mild exposure during the following autumn may furnish a sufficient protection. Inasmuch as the recovery from even severe attacks of Texas fever is usually complete and not followed by any permanent debility, such mild attacks would not be likely to cause any permanent injury to the exposed animals.

Another method of inducing Texas fever is the injection of blood from cases of Texas fever. Such inoculations are apt to result in a mild attack if practiced after the hot weather of mid-summer. The blood of Southern cattle will serve the same purpose, as our experiments carried on this year (1892) have shown. If practiced in early summer the injection of such blood induces a prolonged attack and may cause death. These latter methods of inoculation require either the presence of Texas fever or of freshly imported Southern cattle.\* The former method of exposure to ticks is on the whole simpler, since it requires no operation, and since ticks are easily procurable from the permanently infected Southern territory. Mild attacks of this kind should be watched with care, and the blood examined from time to time to obtain positive information concerning the severity of the induced attack. The temperature should likewise be taken morning and evening.

Efforts to protect Northern cattle by inoculation were made by Dr. Paul Paquin (9, p. 14). We can not review these experi-

\* Since the above was written we have determined that the Texas fever parasite was carried in the blood of a North Carolina animal three years after leaving the permanently infected territory.

ments in detail. While we must commend the faithful work we must dissent from the method, and hence can not regard it as applicable in practice. The wholly different outcome of our experiments concerning the microorganism and the cattle tick as probably the only transmitter prevents us from accepting any results based upon hypotheses which are now shown to be unfounded. But if we look at the results obtained by Paquin's vaccination we will be convinced that they are far from being satisfactory. Thus Dr. Dinwiddie (9, p. 23) reported a mortality of 100 per cent among nonvaccinated animals, and of 75 per cent among vaccinated animals exposed in Arkansas. Of vaccinated and nonvaccinated cattle sent to Texas 66 $\frac{2}{3}$  per cent of the former, and 88 $\frac{2}{3}$  of the latter, died. These percentages show so little difference between the mortality of vaccinated and nonvaccinated cattle that, bearing in mind the various unknown factors which come into play in such experiments, we may regard the effect of this mode of vaccination as negative. What is meant by the author when he speaks of the virus used in (p. 279) these inoculations as doubtful it is difficult to understand. A culture always contains a definite kind of bacteria, and they are either of the wrong kind or the right kind, and no vaccination experiments should be attempted, or, if attempted, reported without an exact description of the underlying conditions, so that they may be repeated if necessary by others. The real difficulty, however, with these experiments, lies deeper. Vaccination experiments were tried before anything definite was known concerning the nature and causation of the disease, and hence were built on hypotheses of a vague character in place of demonstrated facts. Any reader of the foregoing pages of this report will be satisfied that the diagnosis of Texas fever must now require a careful periodical examination of the blood, and that unless this is carried out the disease may escape observation. Again, all test exposures must be made under precisely the same conditions and not in different inclosures with a doubtful or a variable infection, since we now know that the infection is carried by the newly hatched tick.

The statements made above concerning the possible uses of



mild infections as means of subsequent protection must be regarded as mere suggestions, which may or may not prove of practical utility on a large scale. They are carried out so easily, however, that they may be tried by anyone exercising a certain amount of care.

*Is Texas cattle fever restricted to the American continent?*

Among the disease carried from their natural habitat by intercourse, Texas fever occupies a very prominent position. Existing chiefly as a mild, rarely recognizable, malarial infection in certain regions of our country, it becomes a highly fatal infectious disease when transported beyond its natural confines. The movement of cattle is entirely responsible for the phenomenon. The question naturally presents itself whether such a disease is not to be found in other countries situated as we are. Only an active movement of cattle, such as took place in our country in 1867 and 1868, in the hot months of the year, together with their dissemination over Northern pastures, would demonstrate the presence or absence of such a plague on other continents. But there is evidence even now that a disease resembling Texas fever very closely, if not actually identical with it, exists in Southern Africa and in Europe along the Danube.

*South Africa*

In 1883, a report was presented to the English Parliament by a commission of inquiry concerning a disease among cattle in the colony of the Cape of Good Hope known as "redwater." This disease is defined by the commission as—

an infective and malignant fever in horned cattle, characterized by the passing of urine of a color varying from blood-red to purplish-red, and holding the haematin or coloring matter of the blood in solution. One ox can not give another redwater as a smallpox patient can give his disease to his neighbor. Redwater is not contagious in that way. The poison of redwater passes from a suffering animal on to pasturage. What, if anything, happens to the poison at this stage is not fully determined. Another ox feeds over the pasturage thus contaminated and becomes in his turn the sufferer.\*

\* Supplementary report (1884), p. 3.

The disease was first observed in 1870. Since then it has been introduced from time to time by oxen used as carriers, which keep up communication with the territory north of the colony. Of the precise manner (p. 280) in which the virus is communicated by the cattle only this was known, that while they did not infect other cattle directly they did infect the ground over which they passed.

The symptoms of this disease are summarized by the commission as follows:

The beast when first observed, appears dull and sluggish, with a tendency to leave the rest of the herd; the hair stands erect, like that of an animal on a cold day (a staring coat); the ears hang, and the eyes have a dull, lusterless appearance. In some cases the beasts will cease feeding; in other cases they continue to nibble at the herbage until nearly the last, but in an indifferent manner, indicating that they have no relish for their food. There is generally a dribbling of saliva from the mouth; the nose or muzzle may appear quite moist during the early stages of the disease, but it invariably becomes dry and crusty as the disease advances. Later on, the animal will manifest a disinclination to move, and when compelled to do so, will walk with a dragging, straddling gait, as if weak across the loins. In some cases where the sick beast is left undisturbed, it will remain almost constantly in one place, and while standing with head depressed, and ears hanging, in a drowsy, semicomatose condition, look the very picture of complete nervous prostration. Some such cases will lie down the greater part of the time and scarcely move, and when found dead the head and limbs will be resting in their natural position, as if the beast was asleep. In one very marked case of this kind the colonial veterinary surgeon, on making a post-mortem examination, found the carcass pale and almost bloodless, as if the animal had been bled to death. In other severe cases a twitching and quivering of the muscles will be observed, especially of those situated in the flank and behind the shoulder, while the animal will stand and grind its teeth and curl up its upper lip. The beast's dung during the early stages of the disease is very often soft, with a tendency to diarrhea in some cases; but it almost invariably becomes hard as the disease advances. In some very severe cases, where recovery has taken place, the favorable crisis appeared to be ushered in by a salutary diarrhea. But whether the dung is hard or soft it is generally of a brownish tinge, and mixed with blood and mucus. In

milch cows the very first symptom observable is the sudden cessation of milk; and in many mild cases, of which there is generally a considerable percentage in a herd, the only symptoms discernible are a dull, dejected appearance, staring coat, and a slight stiffness for a day or two, after which these symptoms disappear, and the animals resume their usual appearance. Of course, the most prominent and diagnostic symptom in this disease is the color and the character of the urine, which varies generally, as the disease advances, from a pale yellow to a dark port-wine color; in many very typical cases, however, even amongst those which terminate fatally, the urine does not acquire that deep tinge. In many cases, also, even when the attack has been very severe, when the crisis is passed, recovery is very rapid, and it is very remarkable, in such cases, how soon the urine reassumes its normal color and density with the disappearance of the albumen. In other cases, again, where the liver fails to resume its healthy function, the beast will become hidebound and unthrifty-looking, while a thick scurf will form on the skin.

The lesions observed on post-mortem examinations were reported by the veterinary surgeon of the colony as follows:

On cutting through the skin the flesh is seen to be pale and bloodless, and occasionally of a yellowish tinge; sometimes there is a subcutaneous emphysema and infiltration of yellowish-colored serum. . . .

*Liver.*—This organ is nearly always more or less affected, being augmented in volume, and in many instances altered in texture, and so softened as to be easily broken up with the finger. On cutting into it the ducts are often found filled with bile, and sometimes from the cut surfaces large quantities of black blood escape. The gall bladder is usually full of thick bile, and many have thought that this distended condition of it was in some way the cause of the disease, which is quite a mistaken notion, as this state may be observed in other diseases, and in any case where the process of digestion is arrested, as the bile continues to be secreted and simply collects in its natural receptacle till wanted for use.

*Spleen.*—This viscus I have invariably found affected, it being generally enlarged to three or four times its natural size, and filled with black blood, giving to its external surface a livid blue or black color. On holding it up by one end, it will be found that the blood will gravitate to the most dependent part, showing that the splenic tissue is disinte-

grated. On cutting into it, black incoagulable blood escapes from the incision.

*Kidneys*.—In a few instances I have found these organs looking quite natural, but, (p. 281) as a rule, they are much congested, dark in color, and augmented in volume, and sometimes easily broken down.

During the outbreak of this disease in 1871-'72, many persons noticed engorgement or discoloration of the tissues surrounding the kidneys, while the capsules of the kidneys contained a fluid more or less dark colored.

*Bladder*.—This usually contains urine of a high color, often quite black, but sometimes not much altered in appearance. If left to stand it deposits a sediment, which on examination, is found to consist of mucous corpuscles, hippurates, etc., while the urine itself contains a variable quantity of albumen.

The color I find due to the escape of the hematin of the blood.

*Mouth*.—On the tongue I have sometimes seen dark-colored spots or patches, but this condition is by no means constant, as in many instances the mouth looks quite healthy.

*Rumen*.—In this stomach, I have found the inner coat much discolored after the animal has been dead some hours, the epithelium peeling off readily. In other cases when I have opened animals immediately after death, I have not found this condition, though in a few instances I have noticed a slight redness.

*Reticulum*.—This stomach has not exhibited any symptoms of disease in any animal that I have examined.

*Omasum (third stomach)*.—In most cases I have found this organ healthy; some times I have noticed the leaves slightly reddened, and the vessels radiating from their attached border injected, but I have never observed the sloughing which occurs in cases of rinderpest, and some other disease, nor ecchymosis either. When I have found the tissues discolored and the epithelium peeling off readily, it has been after the animal has been dead some time, and the same occurs in cattle which have died from other causes. In a few instances I found the contents hard and dry, in others quite soft.

This dry, impacted state is not peculiar to this disease, nor has it anything to do with the cause of it, as some have supposed.

*Abomasum (fourth stomach)*.—I have noticed intense congestion of this organ in all cases, with more or less ulceration penetrating to the muscular coat. In some instances there were superficial erosions not extending to the submucous tissue.

The mucous membrane was covered with mucus generally tinged with blood.

*Intestines.*—The small intestines are invariably congested, and in other respects present the same appearance as the fourth stomach. Peyer's glands I have found enlarged and dark in color, but I have not detected ulceration of them.

The large intestines present a similar appearance to the small, but in a lesser degree.

In a few instances a kind of croupous exudation has been seen, and casts of portions of the intestines have passed with the feces.

*Chest.*—In this cavity I have not observed any particular indication of disease, with the exception of patches of ecchymosis in the lining membrane of the heart.

*Brain.*—In the few instances where I have examined the brain I have found the membranes covering it much injected, and yellowish colored serum in the ventricles.

Enough of the report has been quoted to illustrate the striking similarity of this South African disease and Texas cattle fever as regards the symptoms and lesions and the non-contagious character of both maladies. Both are carried by cattle from warmer, permanently infected territories, and in both the pastures become infected. In fact, the commission reports that a certain line exists which represents the boundary of the infected district. This is deducible from the minutes of the proceedings, where the following passage occurs:

The commission recommend that the southern redwater line, at present drawn at the Umtata River, be strictly respected, and that no cattle, either loose or in yoke, be allowed to cross that line except from a portion of East Pondoland, where no redwater is known to exist, and from such portion of East Pondoland only by certificate.

It is to be hoped that this peculiar disease will be soon made the subject of investigation to determine whether or not it also is transmitted by some specific parasite like the cattle tick, and whether or not it is really the same as Texas fever.

### *Roumania*

Still better evidence of the existence of Texas cattle fever outside of our own country is furnished by certain investigations

made by Prof. (p. 282) Victor Babes,\* of Bucharest, in 1888, concerning epizootic haemoglobinuria among cattle in Roumania. According to Babes—

A peculiar disease devastates, since olden times, the herds of Roumania. Native veterinarians have given it the name gastro-enteronephritis. Nowhere are references to be found in publications concerning this plague, which formerly was regarded the same as rinderpest. It is not less fearful than the latter in the persistence with which it demands annually thousands of victims from among the most powerful draft oxen, especially in the swampy lowlands of the Danube River. . . . Government commissions had endeavored to determine the nature of the plague in former epizootics, but neither the infectious nor the contagious character could be determined. The disease was looked upon as a kind of malarial disease.

Its dissemination seems to be largely due to draft oxen. Babes is inclined to consider it as spreading from public drinking places, and that the infection starts from such fountains as centers and extends over a restricted area therefrom. Babes also makes the curious statement that "the disease moves from one end of the village to the other, reaches after a few days a certain place in the village from which it does not spread farther, while those animals in the infected part of the village hitherto spared from the disease may succumb later." It is evident that the way in which the virus is disseminated is not known, and that the above statements are more or less contradictory and need elucidation. It should be borne in mind that the conditions as described by Babes must be very complicated, owing to the employment of draft oxen moving from place to place. No mention is made in these investigations of any ectoparasites.

*Symptoms.*—The most powerful draft oxen are the chief victims. Cows are rarely attacked; calves never. An animal affected with the disease appears weak, the head and ears droop and the back is arched. The temperature is elevated, the pulse and respiration rapid. After two days some recover, others begin to pass dark-red urine. In such cases emaciation becomes

\* Die Aetiologie der seuchenhaften Hämoglobinurie des Rindes. Archiv. für pathol. Anatomie und Physiologie, CVX (Jan., 1889), p. 81.

marked, muscular tremors appear, and the temperature rises to 40-41°C. (104°-105.8°F.). The animal now sways and drags its hind limbs after it. The bowels may be constipated or pass liquid, reddish brown, sometimes bloody stools. The disease may terminate fatally in four to seven days. In rare cases fatal relapses occur after apparent recovery. The urine contains but rarely red corpuscles. Usually albumin and coloring matter of the blood are present.

*Pathological changes.*—The lesions found by Babes are intermingled with those produced by *Pentastomum*, so that it is difficult to determine which are due to the specific fever and which to the parasites. Of the more important we may extract the following brief statements:

The lungs may be the seat of emphysema and hyperaemia. The heart muscle is pale red, friable. The fluid blood and the clots in the heart cavities are quite pale, indicating a marked loss of coloring matter. The liver is enlarged, in some cases yellowish brown, in others dark brown and rich in blood. Babes dwells upon the peculiar mottled appearance of stained liver sections due to the fact that the central zone of each acinus is in a necrotic condition; i.e., the nuclei have wholly or partly disappeared from the parenchyma cells. This condition is precisely similar to that observed in Texas fever. The gall ducts are not obstructed. The gall bladder contains fluid, orange-yellow bile.

The spleen is always enlarged, black or blackish red, the capsule tense. The enlargement resides in the pulp, which is blackish, disintegrated.

(p. 283) The third stomach is impacted. The fourth or true stomach is always hyperaemic. As a rule hemorrhagic erosions are found in the pyloric portion, still more frequently flat or deep excavations are observed along the mucous folds, with hemorrhagic base, and covered with a slightly elevated greenish-brown slough, more or less easily removable. The hemorrhagic and oedematous changes along the digestive tract and its mesenteries seem to be much more pronounced than in Texas fever, but, as stated above, *Pentastomum* may have something to do with these.

The kidneys are surrounded by hemorrhagic, oedematous tis-

sue. Frequently the site of a kidney is indicated by a large blackish, hemorrhagic area. The kidneys are enlarged, the cortical portion dark red. In the pelvis more or less extravasation of blood. The bladder contains much dark-red urine.

The musculature of the body is in parts pale and friable. The membranes of the brain and spinal cord are injected, the nervous tissue rich in blood, sometimes softened and oedematous.

That portion of the work most interesting to us is the description of bodies within the red corpuscles, which are strikingly like the parasite of Texas fever in its intermediate stages. Babes finds peculiar microorganisms, which he calls bacteria within the red corpuscles in the capillaries of the mucosa of the stomach and intestines, in the mesenteric glands, in the liver, spleen, and kidneys. In the mesenteric glands they were found free in masses. In the kidneys they were exceedingly abundant, both free and within red corpuscles. He also detected them in the musculature of the body, sometimes in the marrow of the bones. In the brain and spinal cord they were not found.

Babes describes these peculiar microorganisms when stained in Löffler's methylene blue or methyl violet as squarish bodies, each divided by a light line so as to form a body like a diplococcus. The description is vague, but an examination of the illustrations shows that the corpuscles may contain two such diplococci hanging together at one corner and making an angle with each other. Babes finds also that these organisms can not be stained in sections by the current bacteriological methods. He resorts to the following procedure to avoid the decolorizing action of the alcohol: The sections are stained in Löffler's methylene blue for one hour, then dehydrated in an alcoholic solution of methylene blue. Thence they are transferred to an alcoholic solution of eosin and lastly to aniline oil and xylol.

The author believes that owing to the massing together of the "diplococci" in the mesenteric glands, the capillaries of the mucosa of the stomach and the oedemas surrounding these organs, that they enter by way of the ulcers of the fourth stomach, become disseminated in the blood, and then attack the red corpuscles. The probable truth of the matter is, however, that



the bodies which he saw have already been in corpuscles and have been set free by their breaking down.

Bacteriological observations were made on a certain number of cases, of which some are reported. The whole work is regarded as preliminary, however, for the results are by no means conclusive. Several kinds of bacteria were isolated from oxen which had succumbed to the disease. One of these was cultivated with great difficulty, and is fatal to rabbits in about two weeks. Its relation to the disease, though assumed by the author, is not yet proven, since no inoculations are reported which show that it is capable of reproducing the disease in cattle.

In a more recent communication\* Babes gives some additional facts bearing on the microorganism of this disease.

(p. 284) The parasites are quite polymorphous. The characteristic form is that of a diplococcus in the interior of the red corpuscle. In other cases there are two or even three pairs of the microorganism in red corpuscles. The size of these bodies varies. Some individuals are  $2\mu$  others  $0.5\mu$  in diameter. In the fresh condition they are recognizable within the red corpuscles by their moderate refrangibility and their colorlessness. They do not move within the corpuscles. Stained with methyl violet their interior shows a peculiar line of division. The microbes are more tubular (tubisch), with ends rounded off, and they often hang together by means of a fine thread. Stained blue, the bodies are spherical and the chromatic substance is found more on the periphery. The parasites are colored brown in chromate of potash.

It will be observed that this description accords much more closely than the one given in his first communication with that given in this report of the Texas-fever microorganism. Babes has detected no movement or changes of form of the microorganism within the corpuscles. This may be due to the failure to examine the blood during the life of the animal. In fact, his description of these bodies indicates that he has thus far seen them only post-mortem. He also adds the following information concerning the transmissibility of the disease from one animal to another:

\* Verhandlungen des X. internationalen medizinischen Congresses (1890). II. Dritte Abtheilung., S. 104-108.

Blood of sick or dead cattle 2 or 3 days old may still produce the disease, but frequently a considerable quantity of fresh blood does not infect them. Undoubtedly this depends upon other conditions of development of the parasite in the animal body. Thus the parasite can only be transmitted once from cow to cow, and inoculations from rabbit to rabbit can only be carried through two or three generations with success. Of twelve inoculated beeves only four contracted the disease.

In our experiments the infectious agent has been transmitted from a Southern cow to a Northern cow, and from this subsequently to four other Northern cows without any diminution of virulence. In fact, three of the four died. As the evidence for the above statement of Babes, that the transmission of the disease can be effected but once from cow to cow is not presented, we can not examine into it more closely.

As to the cultivation of the microorganism, Babes is more cautious in his statements in this second communication. Of 200 inoculated tubes only 12 showed a feeble growth of diplococci of various sizes. These are said to produce the characteristic disease in rabbits with a hemorrhagic oedematous exudate of the peritoneum and great masses of parasites in the same, exceptionally in blood corpuscles. This sounds more like the more chronic forms of the ordinary *septicæmia hemorrhagica* in rabbit. As to the nature of the microorganism Babes now hesitates to express an opinion, and inclines to the view that it may stand between the bacteria and the protozoa.

It is difficult not to come to the conclusion that this disease is identical with Texas fever. The pathological changes are almost precisely the same, and any minor differences are explainable by the assumption that Babes may have largely examined animals after the acute attack had passed away. The microorganisms of both diseases, and their general appearance and habitat, are strikingly alike. The fact that Babes cultivated his organism and produced disease in rabbits is not a strong argument against their identity, for it seems very probable that he may have had under observation one of those not very uncommon bacteria accidentally associated with various disease processes whose form

is too small to resemble anything in particular and the cultivation of which is attended with many failures. Such forms are familiar to most working bacteriologists. It is nevertheless impossible to come to any positive conclusion that the Roumanian and the American diseases are the same until the investigation concerning the former are carried beyond the preliminary stage in which Babes has left them.

(p. 285) In the Caucasus\* there prevails a disease during the hot season which is called "Tschichir," a name also applied to a kind of red wine, because the urine of affected cattle is red in color. The disease is said to kill thousands of the best cows and oxen annually, and peasants lost the major part of their stock in a few days without being able to do anything to check the disease. The details concerning the disease are very meager. "At first the animal is dull, with drooping head and ears. It clamps its teeth, moans, and discharges from its mouth a viscid, foul-smelling mucus. The bowels may be loose or costive and the urine is bright red." From observations of the disease the following conclusions are drawn:

The "Tschichir" has no infectious properties. The disease attacks mainly working oxen, more rarely milch cows, and never young animals. It is more severe and acute in spring than in fall. It does not last more than three weeks in any one locality. In the first week it begins to show itself, in the second it is at its height, and in the third it disappears completely. The flesh of animals which have died of this disease is consumed without any ill effects by the nomadic tribes of the Caucasus.

#### PRACTICAL OBSERVATIONS AND CONCLUSIONS

It will undoubtedly be conceded by all impartial readers of the foregoing pages that the economic value of the results derived from these investigations is very promising. As yet they are undeveloped, however, and their true importance can not be estimated. Experiments must be built upon them in various directions. These we have thus far been unable to undertake, owing

\* T. Praktische Bemerkungen über die im Kaukasus Tschichir (Haematuria) genannte Krankheit des Hornviehs. Med. Ztg. Russlands, St. Petersburg, 1853, x, 209.

to the large amount of labor involved in determining the relation of ticks to the disease. In the following pages, in addition to deductions immediately available in the control of this disease, a few suggestions are made in regard to the objects to be attained by further investigations and the manner in which they should be conducted. Those readers technically interested in carrying on such investigations will undoubtedly have read between the lines of the foregoing chapters all that can be suggested here.

#### DIAGNOSIS

One of the immediate results of the work is the simplicity and ease with which an outbreak of Texas fever can be positively determined. Most veterinarians and pathologists are able to recognize Texas fever when an acute case presents itself for post-mortem examination. The greatly enlarged spleen, the peculiar coloration of the liver, the thick bile, and especially the haemoglobinuria, are so obvious that no one trained to a knowledge of the appearance of the healthy organs and excretions in cattle can make a mistake. But all cases are not in the acute stage at the time of death, and one or several of these important pathological changes may be missing or barely recognizable when present. In fact, there may be no animals which can be sacrificed, and all may be on the road to recovery. In such cases even the clinical signs, such as the high temperature, may be missing.

Among the diagnostic characters to be added to the list are the examination of the blood and the presence or absence of the cattle tick (*Boophilus bovis*). We may now consider it demonstrated that Texas (p. 286) fever outbreaks in the North are not possible without the cattle tick. Isolated cases may occur through other agencies, perhaps, but no general infection of fields or pastures is possible without the cattle tick. Hence, in any doubtful disease where Texas fever is suspected, ticks should be looked for, and in doing so all those facts concerning the size of the ticks on animals in the acute stage and during recovery and their location on the body must be borne in mind. On animals which have passed through the disease the ticks are nearly or quite full-grown, and

therefore easily detected. But even when great care is exercised the ticks may be overlooked, or in a late fall infection they may have speedily disappeared. In such cases the examination of the blood will give the necessary information. This requires some skill, and a good microscope with objectives and oculars giving a magnification of not less than 500 diameters is necessary. The method of examination as well as the pitfalls to be avoided in interpreting appearances under the microscope have been discussed at length, and need not be again referred to here. While the presence of the microparasite within the red blood corpuscles, and the changed size and appearance of many of the corpuscles themselves, are usually of sufficient diagnostic value, it is always desirable that the number of red corpuscles be estimated at the same time.

In the microscopic examination of the blood attention should be paid, first of all, to the presence of the various stages of the microparasite. In the mild type, the minute coccus-like body will be found within the corpuscle, near its periphery. As it is rarely seen in fresh preparations, stained preparations should invariably be examined. In the acute type of midsummer, associated with high fever, the larger, paired, pyriform bodies are always present but usually in very small numbers. They may be detected as readily in fresh blood carefully mounted as in dried and stained preparations. Next in importance to the microparasite of the disease are the changes induced in the blood corpuscles by the anaemia. In fresh blood the variation in size of the individual corpuscles and the very large size of many (from one and one-half to one and three-quarters times the diameter of the normal red corpuscles) is at once apparent. In properly stained preparations the peculiar granulations and the diffusely stained appearance of a greater or smaller number of the larger corpuscles, as depicted on Plate IX and other plates, is quite characteristic. These changes may, of course, be the result of very severe, repeated hemorrhages, and these must be excluded first before the former can be considered as due to Texas fever. The changes in the blood corpuscles may be directly associated with the parasite in the mild type, but they usually follow the

parasite in the acute type. Hence they may be the only indication of disease recognizable under the microscope in some cases.

A reduction in the number of corpuscles is a very reliable sign of Texas fever. If we except the occurrence of severe hemorrhages and the feeding of chemical poisons, their number is but slightly, if at all, influenced by disease of various kinds. In several cases of advanced tuberculosis no reduction was noticed. In fact, there seems to be but little specific action of bacterial poisons on the red corpuscles, while the Texas-fever microbe limits its destructive action entirely to them. Anaemia in cattle seems to be rare, as we found it but once among the many cases under observation. Hence the counting apparatus is of great service in detecting Texas fever in all its phases, and should be used whenever possible.

A summary of the diagnostic characters to be looked for when this (p. 287) disease is suspected would include among others the following salient ones:

- (1) Cattle ticks.
- (2) Gross pathological changes: Haemoglobinuria; enlarged spleen; enlarged, yellowish liver; thick, flaky bile; ecchymoses on the external and internal surfaces of the heart.
- (3) The microparasite within the red corpuscles.
- (4) Modified or changed corpuscles (enlargement, the presence of stainable granules, etc.).
- (5) The reduction in the number of red corpuscles.

#### PREVENTION

Texas fever in the territory outside of the enzoötic region is the result of the distribution of ripe egg-laying ticks by cattle from the enzoötic region. Hence such cattle should not be allowed on uninfected territory during the warmer half of the year. It is also evident that all cars carrying Southern cattle contain a larger or smaller number of ticks which have dropped off during the journey, and which are ready to lay their eggs. The sweepings of such cars, wherever deposited, may give rise to a crop of young ticks, and these, when they have access to cattle, will produce the disease. Wherever Southern tick-bearing

cattle are kept within twenty-five to thirty days after their departure from their native fields they are liable to infect such places, since it requires the period mentioned for the smaller ticks to ripen and drop off. But under special conditions even this period is too short and the Southern cattle may remain dangerous a longer time. This would occur when such cattle remain in any one inclosure long enough (four to five weeks) for the progeny of the first ticks which drop off to appear on the same cattle.

The above points are covered in the regulations of the Department of Agriculture concerning cattle transportation. These regulations insist on the complete isolation of cattle coming from the permanently infected territory between March 1 and December 1 of each year, and on the proper disinfection of the litter and manure from such cattle during transportation. Furthermore, such cattle can only be transported into uninfected territory for immediate slaughter during the prescribed period. These regulations, if properly carried out, would prevent the appearance of Texas fever at any time in those areas north of the enzoötic territory. The only question which now presents itself with reference to them is the efficiency of the prescribed disinfection. It has been shown that the infection resides only in the cattle ticks and their eggs; hence the destruction of these is absolutely essential to make the disinfection of any value. In the present report this question has not been touched upon; therefore, pending the trial of various disinfectants, which is now going on, any discussion or any suggestions are of little value.

The harmlessness of Southern cattle after being deprived of the cattle tick brings up the very important question whether such cattle can not by some means be freed from ticks so that their transportation may go on without any restriction during the entire year. There are several ways in which experiments might be undertaken. Cattle might be subjected to disinfecting washes of various kinds, or else they might be run through disinfecting baths which expose the whole body to the action of the liquid used. Such processes would require careful attention. (p. 288) The survival of a very few ticks might lead to serious consequences, since a single ripe tick averages about 2,000 eggs.

Cattle may be deprived of ticks on a large scale without the

use of any disinfection if the following plan be adopted: Two large fields in a territory naturally free from cattle ticks are inclosed. The tick-bearing cattle are put into the first inclosure and kept there about fifteen days. They are then transferred to the second inclosure for the same length of time. Thirty days after the beginning of their confinement they may be considered free from infection. The reason for this procedure is simple enough. The cattle drop the ticks as they ripen in the inclosures. By being transferred to a second (or even a third) inclosure they are removed from the possible danger of a reinfection by the progeny of the ticks which dropped off first. It is evident that such inclosures can only be used once a season, since the young ticks subsequently hatched remain alive on the ground for an indefinite length of time. Such inclosures must not be located where there is a possibility that the ticks might survive the winter.

For cattle which are introduced into the enzoötic territory two modes of prevention may be adopted. Either they are kept entirely free from ticks by confinement in stables or upon pastures known to be free from ticks, or else they are exposed to the infection in such a way as to become insusceptible to it after a time. The first method is open to the objection that ticks may at some time accidentally gain access to such cattle and produce a fatal disease. The second method seems the more rational, provided it can be successfully carried out. We know that Southern cattle are insusceptible to the disease, and the way in which this insusceptibility has been acquired has been already discussed (p. 273). Young animals seem to be largely proof against a fatal infection, although they are by no means insusceptible. The repeated mild attacks to which they are subjected finally makes the system indifferent to the virus. The introduction of young animals into the permanently infected territory though not without danger, is far safer than the introduction of animals older than one year. The danger of a fatal infection increases with the age of the animal, and is very great in cows over 5 or 6 years old, as is distinctly shown by the experiments recorded in this report.

The subject of preventive inoculation has already been dis-



cussed and experiments cited on another page. It has been shown that while in general two mild attacks may not prevent a third attack, this will not be fatal. One very acute attack will usually prevent a second severe attack. Hence it is possible to prevent cattle, even when fairly along in years, from succumbing to a fatal attack by several preliminary carefully guarded exposures to a mild infection. This infection may be produced by scattering ripe ticks in an inclosure, or by placing young ticks on cattle in the fall of the year (p. 278). Protective inoculation of this kind should be carried on at some locality outside of the enzootic territory carefully chosen for the purpose. A few years of careful experimentation would probably lead to an efficient method which, when definitely formulated in all its details, could be applied in different parts of the country. Such experimentation should, of course, pay special attention to the relative susceptibility of the various higher grades of cattle, a matter which we have been unable to touch upon thus far.

What can the individual farmer or stock-owner do in the event that Texas fever has been introduced into his pastures? From what has been said thus far pastures which have been infected by Southern cattle (p. 289) or ticks from the litter and manure of infected cattle cars should be avoided during the entire summer season. While we know that young ticks may remain alive in jars for two or three months without food, it would be premature to conclude that such is the case on pastures, as the conditions are quite different. Yet everything seems to point to a long sojourn of young ticks on infected fields, and pending the carrying out of experiments to test this question we would recommend that native cattle be not allowed to graze on infected fields until after the first frosts, for even a mild attack in fall before the ticks have been destroyed by frosts is debilitating to cattle. The period of time during which infected localities remain dangerous varies, of course, with the latitude, and would be shorter the colder the climate.

The infection of stables, stalls, and other structures with the ticks should be counteracted by thorough disinfection. The adult ticks and the eggs must be destroyed. As stated above,

we know as yet very little concerning the agents which will destroy the vitality of the eggs of ticks, but the use of water near the boiling point may be sufficient, if liberally applied, to destroy the life of the embryos. In the case of litter and manure heaps the thorough saturation with some strong mineral acid in dilution may accomplish the purpose. Ordinary lime, slaked or unslaked, densely sprinkled over infected places, so as to form a continuous layer, may be recommended. The slow incrustation of the egg massed with carbonate of lime may be expected, provided the manure is under cover. Otherwise it will be washed away and may leave the eggs unharmed. In regions outside of the enzoötic territory the absence of ticks may be accounted for by the severity of the winter; hence in unprotected localities disinfection is unnecessary after the winter has set in. But it may occur that in sheltered places the eggs will winter over and the ticks reappear the following spring. Whether such ticks are likely to produce any serious trouble in the absence of Southern cattle we are unable to state definitely. All that we know is that disease may break out when Southern cattle of the preceding year are in the pasture, as was demonstrated accidentally in our investigations during 1891. Hence all infected material should be freely exposed to the frost, even though treated with disinfectants beforehand.

#### TREATMENT

If the disease is suspected in a herd, the animals should be searched thoroughly for the presence of small ticks, and the temperature of every animal taken with a clinical thermometer with which every stock-owner should be provided. This, which would be 5 inches long, is inserted well into the rectum and held there three to five minutes. If the temperature is  $104^{\circ}$  to  $107^{\circ}\text{F.}$ , fever is present. The combination of ticks and fever, or the presence of the former in a locality where they do not naturally exist, may be considered a sure sign of the imminence of Texas fever. Though there are at least two species of ticks regularly infesting cattle in the permanently infected territory, these remarks can apply only to the species described in this report, since we know

nothing as yet of the fever producing capacity of the other species (*Amblyomma unipunctata*).

In case the ticks are found on the cattle they should be carefully removed and the cattle transferred at once to uninfected grounds. The cattle should be repeatedly examined for ticks and all found destroyed. While the change of pasture and the removal of ticks may not prevent the attack, nor cut short the disease after it has once shown itself, we feel certain that fewer animals will succumb to it. A single infection is sufficient to cause severe and prolonged disease, as is shown by the injection of infected blood; but the mortality seems to be lower than in natural exposures, where the infection is intensified with every additional tick.

We are unable to recommend any specific remedies to be applied after the disease has appeared, because none have been tried as yet. Quinine and its various preparations fed or injected under the skin may prove of value in destroying the parasite, or perhaps methylene blue, recently recommended for malaria, may be of some service. We hesitate, however, to do more than suggest these remedies, since their efficiency should first be carefully tested by well-planned experiments, which should only be undertaken on a large scale, with a sufficient number of control animals, and guided by a repeated examination of the blood.

The general indications to be followed in attempting to save diseased animals are perfect rest in a sheltered place. Sick animals should not be driven, or excited, for the condition of the circulation is such that any effort may bring about rupture of blood vessels and lead to speedy death. The heart, moreover, is always seriously involved, and should not be strained in any way. Again, the exposure of sick cattle in the sun's heat without shelter is liable to increase the already abnormally high temperature. We have, in fact, observed on unsheltered fields during very hot days a rise of from 2° to 3°F. in presumably healthy cattle during the day, which we must attribute to the effect of the sun's heat. A sheltered place, preferably in the open air, in which the sick animal remains free from the annoyances of other animals, is therefore best suited to its condition. An abundance of pure

water should be supplied to aid the overtaxed liver and kidneys to excrete their abnormal products in a more diluted condition. The food given should be readily digestible. It may be on the whole better to withhold food entirely until the high temperature begins to subside, since the various digestive organs are in a congested state and not in a condition to do any work.

The disinfection of infected pastures is out of the question, and must be left to nature in winter. They may, however, be used for sheep, since we have found these animals unharmed after grazing on them during an entire summer. It is highly probable that all other domesticated animals may run over such pastures with impunity, since Texas fever outside of the bovine species has not yet been observed.

#### CONCLUSIONS

(1) Texas cattle fever is a disease of the blood, characterized by a destruction of red corpuscles. The symptoms are partly due to the anaemia produced; partly to the large amount of debris in the blood, which is excreted with difficulty, and which causes derangement of the organs occupied with its removal.

(2) The destruction of the red corpuscles is due to a micro-organism or microparasite which lives within them. It belongs to the protozoa and passes through several distinct phases in the blood.

(3) Cattle from the permanently infected territory, though otherwise healthy, carry the microparasite of Texas fever in their blood.

(4) Texas fever may be produced in susceptible cattle by direct inoculation of blood containing the microparasite.

(5) Texas fever in nature is transmitted from cattle which come from (p. 291) the permanently infected territory to cattle outside of this territory by the cattle tick (*Boophilus bovis*).

(6) The infection is carried by the progeny of the ticks which matured on infected cattle, and is inoculated by them directly into the blood of susceptible cattle.

(7) Sick natives may be a source of infection (when ticks are present).

(8) Texas fever is more fatal to adult than to young cattle.

(9) Two mild attacks or one severe attack will probably prevent a subsequent fatal attack in every case.

(10) Sheep, rabbits, guinea-pigs, and pigeons are insusceptible to direct inoculation. (Other animals have not been tested.)

(11) In the diagnosis of Texas fever in the living animal the blood should always be examined microscopically if possible.

#### CASES ILLUSTRATING THE VARIOUS PROBLEMS SOLVED BY THE PRECEDING INVESTIGATIONS

From the large number of cases which have entered into the experiments recorded in the preceding pages, a few are selected and given below. The remainder may be found on record in Bulletin No. 1 of the Bureau of Animal Industry, devoted to Texas cattle fever. The cases have been selected to illustrate the various new facts discovered, both with reference to the nature of the disease and its transmission by means of the cattle ticks.

The following brief synopsis will enable the reader to inform himself of the significance of each case:

No. 49 illustrates a severe case of Texas fever with haemoglobinuria, which finally recovered. It was caused by placing the animal in the same pasture with North Carolina cattle.

No. 56 was exposed to the disease several times, and passed through two rather mild attacks.

No. 76 is a fatal case, produced by placing the animal in a field over which ripe egg-laying ticks had been scattered.

No. 102a illustrates the occurrence of Texas fever in calves just born. From the same field as the preceding.

No. 128 illustrates that the disease induced by Texan cattle is identical with that caused by North Carolina cattle.

No. 180 is a fatal case of Texas fever, produced by placing young ticks hatched in the laboratory on this animal.

No. 186 is a fatal case of Texas fever, produced by the intravenous injection of blood from an animal affected with this disease.

No. 198 demonstrates that a fatal case of Texas fever may be produced by injecting into a vein blood of healthy Southern cattle.

(p.295)

*No. 76 (native).*—Heifer 1 year old when received, May 20, 1890, from the District of Columbia.

July 4.—It was exposed in field VIII (cattle ticks only).

August 14.—Temperature, 104.1. Blood corpuscles, 4,966,000. In fresh preparations nothing abnormal detected. Stained preparations equally negative.

August 16-18.—Heifer growing thin and weak quite rapidly.

August 18.—7 a.m. Animal walking about, but very weak and unsteady in its movements. At 9 a.m. lying down, unable to rise. Temperature, 99.7; pulse, 124; respiration, 16. The skin almost bloodless. Blood obtained with difficulty from skin incisions. Corpuscles 3,475,000. In fresh preparations a few double pyriform intraglobular parasites observed. The same detected in stained preparations. As the temperature of the animal was falling rapidly and the animal now unable to rise and evidently dying, it was killed at 11 a.m., by a blow on the head.

*Autopsy:* On the skin of thighs, escutcheon, and belly a large number of ticks just completing the last moult. Lungs normal. Some adult specimens of *Strongylus micrurus* (both sexes) in terminal bronchi. Heart fibers have undergone cloudy swelling. In blood from the right ventricle scarcely any parasites present. Spleen weighs  $1\frac{3}{4}$  pounds; enlarged; capsule tense; under it a few hemorrhagic patches. On section, pulp dark, still consistent, however. In teased preparations some large cells containing from one to four red corpuscles. No free pigment. In stained preparations not more than 1 per cent of the red corpuscles contain the parasite.

Liver weighs  $5\frac{1}{2}$  pounds. Evidently enlarged. Yellowish brown. In fresh sections small areas of the lobules show bile injection, while the fatty degeneration is more or less uniform over the lobule. Occasional interlobular bile ducts appear as yellow streaks. In teased preparations made some hours after death fully 10 per cent of the corpuscles contain apparently round or oval pale bodies from 1.5 to 2  $\mu$  in diameter. These are usually in pairs situated a variable distance apart. In some only one, in others four bodies are seen. In stained preparations made at autopsy the parasites are all pyriform in shape.

About 8 ounces of bile in gall bladder. Specific gravity, 1022. Holds in suspension a small amount of flaky yellow material.

Kidneys are of a uniformly dark-brownish red color throughout. Fresh sections magnified appear dusted over with minute reddish pigment granules. The capillaries everywhere distended with blood corpuscles. In those of the medulla it is easy to see with high powers in fresh sections each corpuscle containing one to four parasites. When cover-glass preparations are stained few corpuscles are present, but everyone con-

No. 49 (native).

[Heifer, 3 years old. Received August 16, 1889, and kept with Nos. 35 and 41 until September 14, when it was transferred to field III (North Carolina cattle with ticks). No indication of disease. Calved February 15, 1890. July 4, 1890, exposed with calf No. 85 in field VI (North Carolina cattle with ticks).]

Date	Number of red corpuscles	Parasites in red corpuscles		Condition of red corpuscles		Temperature	Pulse	Respiration	Remarks
		In fresh preparations	Dried and stained	In fresh preparations	Dried and stained				
Aug. 21, 1890	4,865,000	Some large parasites.	.....	Normal.....	Normal.....	106.7	88	48	Removed to-day with calf to field IV (sick natives only). Urine and feces normal. Losing flesh rapidly.
Aug. 22, 1890	3,579,000	Some bright bodies.	Some large parasites.	.....do.....	.....do.....	106.9	96	63	
Aug. 23, 1890	3,162,000	Negative.....	Negative.....	.....do.....	.....do.....	105.7	90	45	Urine free from hæmoglobin; sp. gr. 1022. Albumen 0.05 per cent.
Aug. 27, 1890	3,050,000	.....do.....	Some large parasites.	Some macrocytes.	Punctated and tinted corpuscles.	101.5	90	45	
Sept. 4, 1890	2,213,000	Large parasites	10 per cent large parasites.	.....do.....	.....	103.8	84	60	Urine has a deep port-wine color. Sp. gr. 1030. Alkaline. Albumen present. Sept. 5, urine contains less hæmoglobin. Sept. 6, urine free from hæmoglobin.
Sept. 2, 1890	3,800,000	A few bright bodies.	Some large parasites.	Many macrocytes.....	.....	102.0	90	54	
Sept. 18, 1890	4,400,000	Many bright rod-like bodies.	Negative.....	.....do.....	.....	102.4	.....	.....	Urine pale, watery. Sp. gr. 1013. Otherwise normal.

Sept. 30, 1890	2,671,000	Some bright, rod-like bodies.	.....do.....	Some macrocytes.....	.....	100.6	78	24	Urine free from abnormal constituents. Sp. gr. 1040.
Oct. 7, 1890	3,521,000	Negative.....	Negative.....	Many macrocytes.....	.....	101.0	90	24	
Oct. 14, 1890	3,722,000	Some pale, rod-like bodies.	5-10 per cent peripheral coeci.	.....	.....	101.6	84	42	Bowels rather loose. Odor of feces disagreeable.
Nov. 8, 1890	4,303,000	.....do.....	Negative.....	.....	.....	.....	.....	.....	Dec. 1. This animal began to lose flesh Aug. 21, and continued to do so until Sept. 5, at which time it was very weak. Since then it has been gradually recovering and has now almost regained its original weight. Temperature very high from Aug. 18 to Aug. 23.
Nov. 19, 1890	4,920,600	Negative.....	.....do.....	Normal.....	Normal.....	103.4	80	40	Not exposed. In field XII during the summer.
Nov. 13, 1891	5,872,000 (white 16,363)	.....	.....do.....	.....do.....	.....do.....	103.2	72	48	



No. 56 (naine)

[Steer, 2½ years old, received from Maryland September 14, 1889, and exposed in field II (North Carolina cattle with ticks) and other fields subsequently].

Date	Number of red corpuscles	Parasites in red corpuscles		Condition of red corpuscles		Tem- pera- ture	Pulse	Respiration	Remarks
		In fresh preparations	Dried and stained	In fresh preparations	Dried and stained				
Nov. 7, 1889	6,040,000	Negative.....	Negative.....	Normal.....	Normal.....	.....	.....	.....	No symptoms of Texas fever up to date; slight loss of flesh. Re-exposed in field VI (North Carolina cattle with ticks). A few small ticks on animal.
Dec. 2, 1889	5,422,000	.....do.....	.....do.....	.....do.....	.....do.....	.....	.....	.....	
Sept. 8, 1890	.....	.....	.....	.....	.....	.....	.....	.....	
Sept. 20, 1890	6,844,000	Some bright bodies	Negative.....	Normal.....	Normal.....	100.8	.....	.....	
Sept. 22, 1890	5,640,000	Many bright bodies.	.....do.....	.....do.....	.....do.....	106	72	60	One mature and several small ticks on animal.
Sept. 29, 1890	5,307,000	A few bright bodies.	.....do.....	.....do.....	.....do.....	102	72	36	
Oct. 9, 1890	5,436,000	.....do.....	.....do.....	.....do.....	.....do.....	101.6	72	54	
Oct. 22, 1890	4,666,000	Many bright bodies.	10 to 20 per cent periph- eral cocci.	.....do.....	do.....	102.3	54	30	
Oct. 25, 1890	2,754,000	.....do.....	.....do.....	.....do.....	.....do.....	103	60	24	
Oct. 30, 1890	2,720,000	.....do.....	.....do.....	Many macro- cytes. 30 per cent macrocytes.	Some punctated corpuscles. 10 to 20 per cent tinted corpuscles.	101.7	72	36	
Nov. 6, 1890	2,344,000	.....do.....	20 to 30 per cent periph- eral cocci.	.....do.....	.....do.....	104.1	60	54	

Nov. 8, 1890	1,984,800	.....do.....	30 per cent peripheral cocci.	.....do.....	.....do.....	104	81	96	No ticks can be detected; steer dull and losing flesh slowly.
Nov. 10, 1890	.....	20 per cent bright bodies	.....do.....	.....do.....	.....do.....	104.2	90	96	Feces yellow; bright intraglobular bodies appear a little larger than before, oval in outline.
Nov. 13, 1890	1,183,000	5 per cent bright bodies.	10 per cent peripheral cocci.	.....do.....	Some hæmato- blasts.	103.2	81	41	
Nov. 15, 1890	1,534,000	15 to 20 per cent bright bodies	.....do.....	20 per cent macrocytes.	10 per cent punctated and 5 per cent tinted corpuscles.	101.9	84	78	
Nov. 17, 1890	1,655,000	1 to 2 per cent bright bodies.	1 to 2 per cent peripheral cocci.	.....do.....	5 per cent punctated and tinted corpuscles.	101.5	68	36	
Nov. 21, 1890	2,615,000	A few bright bodies.	A few peripheral cocci.	.....do.....	.....do.....	102.7	72	36	
Nov. 26, 1890	3,880,000	.....do.....	Negative.....	.....do.....	.....do.....	101.8	72	36	
Nov. 28, 1890	.....	A few bright bodies.	One pair large parasites. (Plate vi, Fig. 4.)	.....do.....	.....do.....	.....	.....	.....	Has lost largely in weight; now improving.
Dec. 2, 1890	4,706,000	.....do.....	Negative.....	Some macrocytes.	=*	102.2	68	40	
Dec. 11, 1890	4,603,400	.....do.....	1 per cent peripheral cocci.	.....do.....	=	103	76	48	December 31. Recovery complete so far as outward appearances go.
July 2, 1891	.....	.....do.....	.....do.....	.....do.....	.....do.....	.....	.....	.....	Re-exposed in field VI (North Carolina cattle with ticks).
Aug. 26, 1891	3,242,000	Negative.....	Negative.....	Normal.....	Normal.....	106.8	68	38	

\* The sign equality signifies the same condition as indicated in the preceding column.

No. 56 (naïve)—Continued

Date	Number of red corpuscles	Parasites in red corpuscles		Condition of red corpuscles		Temperature	Pulse	Respiration	Remarks
		In fresh preparations	Dried and stained	In fresh preparations	Dried and stained				
Sept. 1, 1891	3,553,000	.....do.....	.....do.....	Many macrocytes	=	103.2	60	54	
Sept. 12, 1891	3,264,000 (white 9,434)	Several pairs of large parasites.	.....do.....	.....do.....	=	101.2	66	54	Many ticks on animal.
Oct. 13, 1891	4,687,000	.....do.....	.....do.....	.....do.....	.....do.....	101.2	96	36	
Aug. 26, 1892	6,687,500 (white 15,000)	.....do.....	.....do.....	Normal.....	Normal.....	101.4	60	60	Re-exposed in Field VI (North Carolina cattle with ticks).
Sept. 8, 1892	5,125,000 (white 6,250)	.....do.....	.....do.....	Slight variation of size.	=	102.6	76	48	
Sept. 21, 1892	6,365,000 (white 8,750)	.....do.....	.....do.....	Normal.....	Normal.....	101.2	84	24	Probably a slight attack.

tains a pair of parasites. Besides these there are numerous free bodies identical with those in the corpuscles.

In the bladder about 3 pints of urine containing a large amount of haemoglobin so that it is barely translucent in layers an inch deep. Specific gravity, 1017. Slightly acid. On boiling, a brownish flocculent precipitate is formed. In the slight, amorphous deposit a few short granular casts.

Digestive tract: In fourth stomach the mucosa of laminae pinkish and beset with small elevations having a central hole (worm pits). Numerous specimens of *Strongylus contortus* actively moving. In duodenum specimens of *Dochmius*. Mucosa bile-stained. Worm nodules in ileum. In the upper colon masses of clotted blood in which are imbedded round worms (*Esophagostoma*).

*No. 102a (native)*.—Calf of No. 102. Born September 1, 1890, died September 13; kept in refrigerator until September 15. The examination was delayed because of other work. It was presumed that the calf had succumbed to other causes, but to our surprise the autopsy demonstrated a marked case of Texas fever, as the following notes will show.

*Autopsy*: Several small ticks found on skin of thighs. The subcutaneous, as well as visceral fat over the whole body, has a decided yellow tinge.

Heart empty, contracted. Fatty degeneration of fibers. Spleen (weight 13 ounces) was dark, enlarged and softened. Liver (1 $\frac{3}{4}$  pounds), firm, brownish red. In fresh sections and teased preparations fatty degeneration of the hepatic cells moderate; nuclei distinct. Occasional spots showing bile injection. Considerable number of minute golden needle-like crystals scattered over the section. In stained preparations about 10 per cent of the red corpuscles in the liver contain each a pair of parasites. Bile thick and full of flaky sediment. Not so dark in color as with adults. Kidneys very hyperaemic, of a dark brownish-red color. In fresh sections capillaries distended with red corpuscles. About 20 per cent of corpuscles invaded by parasites.

About 500 cc. (1 pint) of urine in bladder deeply colored with haemoglobin, not translucent in layer three-fourths inch deep. Specific gravity, 1022. Reaction, acid; 1.4 per cent albumen (Esbach).

*No. 128 (native)*.—Cow, 12 to 14 years old. Received July 4, 1892, from the District of Columbia, and exposed in field II, to Texas cattle with ticks.

July 25.—Corpuscles 6,360,000. They appear normal in fresh and stained preparations.

(p. 296) July 29.—Corpuscles 5,673,000. Normal in fresh and stained preparations.

July 31.—Corpuscles 5,820,000. Normal in fresh and stained preparations.

September 1.—Dies at noon and examined at once.

Animal in fairly good condition. Weighs about 650 pounds. A small number of ticks of various stages attached to skin.

Blood from a skin incision examined a few minutes after death. In a considerable number of red corpuscles parasites singly or in pairs. The forms are mostly round, rarely spindle-shaped or pyriform, and their diameter is about one-third the diameter of the corpuscle. In several slight changes of outline observable. Besides these some corpuscles likewise contain each one bright body changing its position rapidly. In the fresh preparations are also noticed very minute bacteria-like bodies moving or dancing about free in the plasma. Whether these are mere debris particles in Brownian motion is not determinable. In stained preparations from 20 to 30 per cent of all corpuscles contain the parasite in its large stage. The majority of the infected corpuscles contain each but one body which is usually roundish, rarely pyriform in outline. Occasionally, however, a group of corpuscles is encountered which contain each a pair of pyriform bodies. All parasites stain feebly and show more or less refrangence when examined in water.

Blood from the external jugular and the heart shows the same features.

Heart: Slight, mottled discoloration of muscular tissue of left ventricle. Considerable extravasation of blood under endocardium. Many sarcosporidia cysts in this situation. Muscular fibers in state of cloudy swelling.

Lungs: Considerable interlobular oedema in both ventral and adjacent portion of principal lobes. In the right principal lobe, near the lateral edge, a mass of tissue  $1\frac{1}{2}$  to 2 inches in diameter partially hepatized with interlobular effusion of serum.

Spleen large, weighs  $4\frac{3}{4}$  pounds. Pulp dark, almost disintegrated. A few intraglobular parasites and much pigment in lumps, either free or intracellular observed in teased preparations.

Liver weighs about 12 pounds. Very much congested, parenchymatous swelling. Bile injection observed in restricted places and fatty changes absent. Numerous infected corpuscles detected in teased preparations.

Kidneys also intensely congested; the whole parenchyma has a uniformly dark brownish-red color. In sections all capillaries gorged with corpuscles, in some of which parasites are noticed. The epithelium of the convoluted tubules contains much pigment in granules. Bladder contains about 3 quarts of urine, having a very dark port-wine color. In a test tube having a diameter of three-fourths inch this urine is practically opaque. When acidified with acetic acid and boiled an abundant precipitate is formed.

Digestive tract: Mucosa of fourth stomach dark pink. Pits due to *Strongylus Osteragi* present, and numerous erosions with a depressed hemorrhagic base, from one-eighth to one-fourth inch in diameter. Considerable hyperaemia of the mucosa of the entire small intestine. Pigment patches in caecum and hyperaemia in the rectum on the longitudinal folds.

This being a very favorable case, examined immediately after death the following cultures were made:

Blood: Peptone-bouillon, peptone agar with and without glycerine.

Spleen: The same media.

Liver: Agar with and without glycerine.

Kidney: The same.

Bile: The same.

The tubes were inoculated from the blood and the bile, with a looped platinum wire, from the organs, with a straight platinum wire.

These various tubes were kept in the thermostat several weeks, but all remained sterile.

On the other hand, stained preparations of the various tissues show the following results as to the presence of the intraglobular parasite approximately stated:

Blood from the skin contains about 20 per cent of infected corpuscles. The parasites are largely in pairs and pyriform. Blood from the right heart contains about the same number. Blood from the jugular contains fewer (about 10 per cent).

Spleen contains from 10 to 20 per cent of infected corpuscles. The parasites roundish, chiefly in pairs.

Liver contains from 40 to 50 per cent of infected corpuscles. There are also mostly in pairs and many are pyriform.

Kidneys contain between 80 and 90 per cent of infected corpuscles. These parasites are nearly all double. Some corpuscles contain three and four parasites. There are also an immense number of bodies not free from disintegrated corpuscles in this organ.

No. 180 (native).—Heifer, age 2 years, received July 25, 1891, from

Maryland. Placed in Field I. From this date to August 4, inclusive, about 20 to 30 young ticks were placed on this animal daily. (p. 297)

July 25.—Temperature, 102.4; pulse, 80; respiration, 48. Red corpuscles, 5,396,800. In fresh preparations a few corpuscles containing bright bodies. Stained preparations negative.

July 31.—Temperature, 104; pulse, 70; respiration, 30. Corpuscles, 4,462,700. Fresh and stained preparations negative.

August 3.—Temperature, 102.0; pulse, 60; respiration, 30. Corpuscles, 4,560,000. Fresh and stained preparations negative.

August 6.—Temperature, 106.7; pulse, 72; respiration, 48. Corpuscles, 4,636,300. Blood examination negative.

August 8.—Losing flesh and becoming weak.

August 10.—Animal very weak and thin. Temperature, 107.7; pulse, 120; respiration, 87. Corpuscles, 1,864,900. In fresh and stained preparations a very small number of corpuscles detected, containing parasites of medium size.

August 12.—Died between 6 and 7 a.m.

Autopsy (9 a.m.). Animal has lost considerable flesh since the beginning of the fever. Weighs now about 400 pounds.

Ticks on the inner surface of thighs, on abdomen, and neck. On the average about one to a square inch. They are still small, about  $\frac{1}{8}$  inch long.

Heart surface well sprinkled with ecchymoses. These are most numerous on the left ventricle. Both sides of the heart contain rather large, dark, firm clots, that in the right being the larger. Considerable blood extravasation under endocardium of left ventricle, especially marked on septum.

Lungs somewhat oedematous.

Spleen weighs  $2\frac{3}{4}$  pounds. Small blood tumors along the course of the vessels under capsule.

Liver weighs 10 pounds; enlarged, edges rounded off. The parenchyma has a yellowish hue. When examined with a lens the yellow coloration is found limited to the tissue around the hepatic vessels. In fresh sections bile injection appears restricted to small areas. Fatty degeneration well advanced. The hepatic cells contain lumps of pigment, and red needle-like crystals are sprinkled over the section. Bile in gall bladder very viscid, and holds in suspension a large quantity of flocculent matter.

Kidneys deeply congested throughout. In bladder 3 quarts of urine, which has a light claret color. Specific gravity, 1018. Acid reaction.

Albumen, according to Esbach, 0.2 per cent. On standing, urates are deposited.

Digestive tract: A few hemorrhages on lamellae of fourth stomach. In the large intestine more or less pigmentation of mucosa. Contents dry and massed into fine balls. Intestines otherwise normal.

In preparations of heart's blood, parasites are rare. They are in general roundish in outline and but one within a corpuscle. In the liver there are about 1 to 2 per cent; in the spleen still less. In one preparation of the spleen pulp a capillary is seen filled with infected corpuscles only. Each contains two parasites. In the kidney not less than 10 per cent of the corpuscles contain either one or two parasites. The large post-mortem bacillus is likewise present in small numbers.

*No. 186 (native).*—Red cow, from 10 to 12 years old, received from Maryland September 4, 1891, and placed in uninfected field II.

September 8.—Temperature, 102.2; pulse, 72; respiration, 48. Red corpuscles, 4,980,700; white, 13,461.

September 19.—From the jugular vein of No. 181, sick with Texas fever, a syringe full of blood (14 cc.) was withdrawn and injected directly into the right jugular of No. 186. The blood of No. 186 was carefully examined microscopically before the injection. In a fresh preparation one minute round body, 1  $\mu$  in diameter, seen in a corpuscle, slightly changing place.

September 25.—Temperature, 106; pulse, 72; respiration, 78. Red corpuscles, 4,761,905. In preparations of fresh blood several corpuscles detected with large pyriform parasites, each with a dark point (nucleus?). In stained preparations none observed.

September 26, 2:30 p.m.—Temperature, 107; pulse, 96; respiration, 108. Red corpuscles, 4,333,300. In fresh and stained preparations a small number of corpuscles containing large parasites.

September 28, 2:15 p.m.—Temperature, 101.2; pulse, 108; respiration, 60. Red corpuscles, 2,123,077; white, 4,615. From 1 to 2 per cent of corpuscles contain amoebiform parasites.

The animal stands trembling and quivering, swaying with her hind quarters, and scarcely able to remain on her feet while a few drops of blood are being collected from a skin incision for examination. Soon after she falls down and remains on the ground.

At 3:30 p.m. a syringe of blood (7 cc.) is withdrawn from a jugular vein to inoculate several pigeons. After this insignificant operation the cow goes into convulsions and dies. (p. 298)



Autopsy notes: Animal has lost much flesh. Weighs now about 700 pounds.

Lungs normal. Heart firmly contracted. Considerable extravasation under the epicardium of left ventricle, much less on the right ventricle. Many ecchymoses and small haematomata under endocardium of both ventricles. Heart muscle shows slight fatty degeneration. In the serum expressed from the heart muscle a large number of large parasites both free and within corpuscles. In stained preparations from 30 to 40 per cent of all corpuscles are infected. Many parasites in pairs. (Plate IV, Fig. 5.)

Spleen weighs  $4\frac{9}{16}$  pounds. Very much enlarged. Tortuous injected vessels on capsule with hemorrhages along their course. The pulp is very dark and very soft. Malpighian bodies invisible. In teased preparations examined fresh there are many large cells containing from two to eight red corpuscles. Two capillaries seen, in which nearly every corpuscle is infected. Pigment present in small quantities. In stained preparations about 8 to 10 per cent corpuscles contain large parasites.

Liver weighs 14 pounds. Some old adhesions on the right between it and diaphragm. Tissue rather firm, color departing slightly from the normal. Yellowish dots and lines are seen on section corresponding to the zone around hepatic veins. In several larger branches of the hepatic vein are thrombi. In fresh sections and teased preparations, bile injection localized to small areas around intralobular veins. In stained preparations from 20 to 30 per cent of the corpuscles infected.

Bile very thick and flaky, holding a large amount of amorphous matter in suspension.

Considerable oedema in the fatty tissue around kidneys. The organs are in a condition of general congestion; all normal markings effaced or indistinct. Glomeruli prominent. Cut surface granular. Many ecchymoses in pelvis. In fresh sections all capillaries choked with red corpuscles. In stained preparations nearly all corpuscles contain parasites. There are also many free forms. In sections of tissue (hardened in Müller's fluid and alcohol and embedded in chloroform paraffin) stained in haematoxylin the engorged capillaries contain only infected red corpuscles (Plate VII, Fig. 2). Structural changes not noticeable.

In bladder, 2 quarts of urine of a dark reddish color. No sediment on standing. Specific gravity, 1015. Feebly acid. About 0.05 per cent albumen (Esbach). Precipitate with acetic acid without heat.

The mucosa of fourth stomach has a bluish red to bright red color. Digestive tract otherwise not affected.

*No. 198 (native).*—Cow 7 years old, received June 3, 1892, from Prince George County Md., and kept on an adjoining farm until June 30, then transferred to field III.

July 6.—Injected into left jugular vein 28 cc. (two syringefuls) of blood drawn from the jugular vein of North Carolina cow No. 217. The transfer of blood from the vein of one animal to that of the other was made in the same syringe and occupied not more than two minutes. The syringe had been warmed previously to 105°F. after being thoroughly disinfected in 5 per cent carbolic acid and boiling water.

The table on the following page gives, in brief, the clinical history of the animal up to the time of death.

(p. 300) Autopsy about one and one-half hours after death. Animal thin; weighs about 600 pounds; has lost about 200 pounds during illness.

Several small areas of intralobular and subpleural emphysema in the principal lobe of both lungs, and in the right ventral lobe. The connective tissue of old pleural adhesions forms a fringe along lateral borders of principal lobes which is in a dark-red hyperaemic condition. A dark red, airless lobule in the right cephalic and the left principal lobe.

Slightly oedematous condition of the fat around heart case. Very marked ecchymosis of the ventricular surfaces of the heart, the discoloration extending in some places from one-eighth to three-sixteenths of an inch into the heart muscle. Extensive extravasation beneath endocardium of left ventricle; slight extravasation in right ventricle. Blood from the heart coagulates promptly in beakers. The serum is much more deeply colored than that from healthy cattle.

Spleen weighs 5½ pounds. Capsule very much distended. Pulp dark brownish, still consistent in texture. Malpighian bodies barely visible on section.

Liver weighs 13¾ pounds (without gall bladder). It is paler than normal and shows a peculiar mottling with irregular yellowish-gray patches, each less than 1 mm. in diameter. On section the organ appears yellowish brown, and the course of the intralobular veins is marked by yellowish-gray borders. In fresh sections fatty degeneration of the parenchyma and the bile stasis quite extensive. Sections were also examined from tissue hardened in Müller's fluid and alcohol. In these after staining with acid haematoxylin or alkaline methylene blue, only a narrow region of the acini bordering on the intralobular tissue was found free from necrotic changes. These were manifested by partial or total loss of the nucleus. The capillaries of these areas were in places very much distended and filled with red corpuscles, many of which contained parasites.

Date	Number of red corpuscles	Parasites in red corpuscles		Condition of red corpuscles		Temperature	Pulse	Respiration	Remarks
		In fresh preparations	Dried and stained	In fresh preparations	Dried and stained				
July 5.....	6,625,000 (white, 8,750)	.....	Negative.....	.....	Normal....	102.5	68	80	
July 7.....	6,291,666 (white, 10,416)	.....	.....do.....	.....	.....do.....	103	56	81	
July 9.....	6,237,500 (white, 20,000)	.....	.....do.....	.....	.....do.....	102.5	58	48	Stands with back slightly arched.
July 11.....	5,925,000 (white, 9,625)	.....	.....do.....	.....	.....do.....	102.2	52	68	
July 13.....	5,187,500 (white, 6,000)	.....	.....do.....	.....	.....do.....	105.2	64	96	Drooping of head and arching of back quite pronounced. Appetite unimpaired; continues to stand most of the time.
July 15.....	5,400,000 (white, 10,000)	.....	.....do.....	.....	.....do.....	104.5	64	80	Falling away in flesh. Very dull.
July 16.....	4,825,000 (white, 7,500)	.....	Several paired and 7 to 8 unpaired parasites.	.....	.....do.....	106.6	56	68	Appetite failing. Loss of flesh continues. Drooping of head and arching of back more marked.
July 18.....	3,112,500 (white, 5,000)	5-10 per cent irregular, roundish parasites, chiefly single.	As in fresh preparation.	Normal....	.....do.....	106.4	96	92	Very dull and weak: Lies most of the time on left side with head extended and resting on the ground. Passes much claret-colored urine at 6 and 11:30 a.m.
July 19.....	.....	.....	.....	.....	.....	.....	.....	...	Found unable to rise at 6 a.m. Dies at 11 a.m.

In the gall bladder about one-half liter of very thick, flaky bile.

The fat around kidneys contains a moderate amount of serous effusion. Kidneys enlarged (left,  $1\frac{7}{8}$  pounds; right, 2 pounds); capsule readily removable. Parenchyma of a uniform dark brownish red. Much serum flows from the cut surface. The glomeruli stand out as minute blood-red points. The tips of papillae hyperaemic and the calices of the pelvis surrounding them ecchymosed. Microscopic examination of fresh sections show extreme engorgement of all blood vessels.

Urinary bladder contains  $1\frac{1}{2}$  liters of urine, having a dark port-wine color and barely translucent in a layer three-fourths inch deep. No sediment on standing.

The second stomach adherent to the diaphragm by means of old connective tissue over an area 6 inches square. This tissue dark red, very hyperaemic. The mucosa of fourth stomach in the laminated portion is of uniformly pink color. The pyloric portion is beset with a number of irregular shallow erosions with hemorrhagic base. They vary from one-half to 2 inches in length, and are elongated in shape. The mesentery of duodenum (near portal fissure) is infiltrated with pale reddish serum. Mucosa of small intestine coated with a pasty bile-stained substance representing desquamated epithelium. Mucosa of rectum congested in patches and containing fecal balls.

The pia covering the hemispheres of the brain injected and pigmented. The plexuses are considerably engorged with blood. No fluid in the ventricles, and no abnormal appearance of the brain substance itself. In sections of the cerebral tissue hardened in Müller's fluid and alcohol, and stained in haematoxylin, capillaries could be traced for some distance in the white substance underlying the gray, which were filled completely with infected corpuscles. From one of the puncta vasculosa on the cut surface of the white substance of the cerebrum, while still fresh, a bit of tissue was crushed under a cover glass. In it a capillary was traced for some distance containing only infected corpuscles. In the choroid plexus of lateral ventricles many of the gorged capillaries are observed containing infected corpuscles only.

Stained cover-glass preparations from various tissues and organs were examined for infected corpuscles with the following results:

	<i>Per cent</i>
Blood from subcutaneous vein, about.....	10
Spleen pulp.....	10
Liver tissue.....	10
Hyperaemic spot on omentum.....	10

	<i>Per cent</i>
Kidneys.....	50
Heart muscle (excluding free parasites).....	30
Brain tissue.....	2-3
Choroid plexus of lateral ventricles.....	10-20
Hyperaemic adhesion of second stomach.....	10
Skeletal muscles.....	very few

The parasites appeared in the red corpuscles, both single and in pairs. The numerical relation, in the different preparations, of single and double bodies varied more or less, the former being in some regions in the majority, in others in the minority.  
(p. 301)

#### DESCRIPTION OF PLATES

Every figure illustrative of red blood corpuscles, containing the parasites or modified by the disease, was made from one field of the microscope, and this only, unless especially mentioned to the contrary, in the descriptions below. The drawings are therefore equivalent to photographic reproductions, in so far as nothing was omitted from the field or inserted from other fields (with exceptions to be given). The slight differences in the coloring are due to the different intensity of the stain in the preparations, and were copied as accurately as possible by the artist.

The preparations illustrating blood corpuscles were all drawn with the aid of a Zeiss apochromatic objective, 2 mm., 1.30 n.a., and the measurements made with the compensating micrometer ocular No. 6. The occasional variation in the magnification is due to the fact that the earlier drawings were made with the draw tube in, the later ones with the tube length so adjusted that each division of the ocular micrometer was exactly equivalent to 2  $\mu$ .

# PLATES

## PLATE I. DISEASED AND HEALTHY SPLEEN.

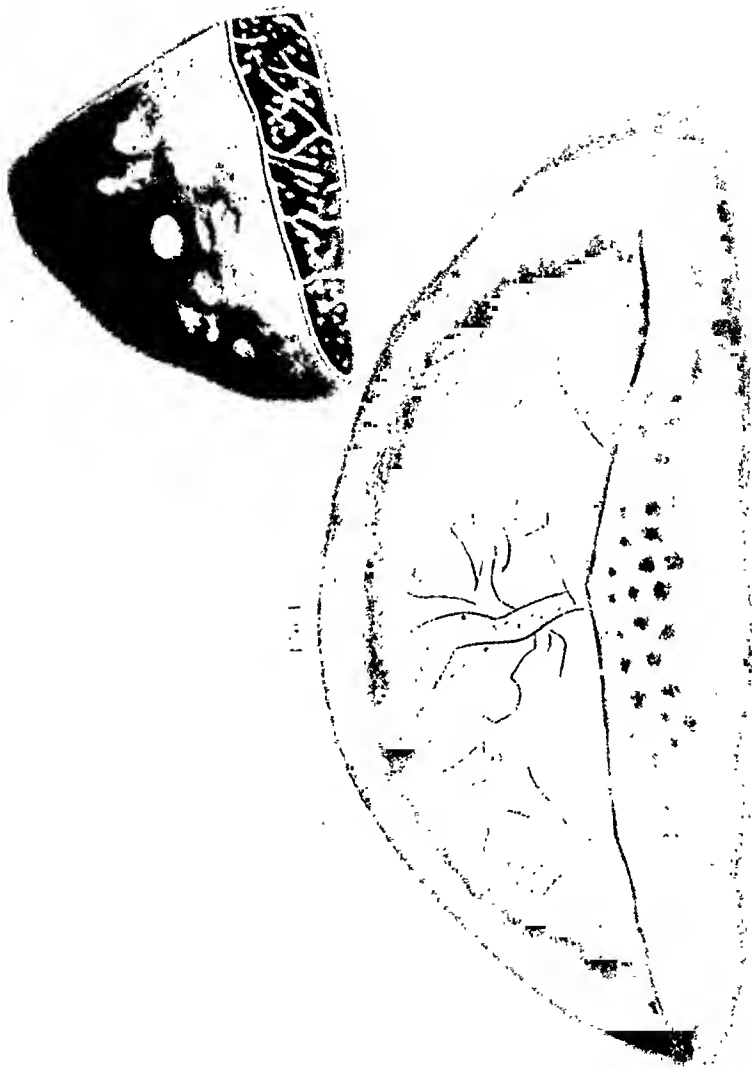
Fig. 1. Spleen of No. 130.\* The smaller ventral end is here represented. Weight of entire spleen  $6\frac{1}{2}$  pounds.

Fig. 2. Spleen of healthy steer killed for beef. The same region selected as in the diseased spleen. Weight  $2\frac{1}{2}$  pounds.

Note the enormous enlargement of the diseased spleen, the almost blackish appearance of the pulp, and the concealment of the trabeculae and Malpighian bodies as compared with the healthy spleen. The ratio of the weight of the diseased to that of the healthy spleen is in this case as  $2\frac{1}{2}$  to 1, while the weights of the animals is as 2 to 3 (800 to 1,200).

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\* Those technically interested in this subject we refer to Bulletin No. 1 of the Bureau<sup>1</sup> of Animal Industry for the complete history of the cases to which these numbers belong.



DISEASED AND HEALTHY SPLEEN



## PLATE II. DISEASED AND HEALTHY LIVER.

- Fig. 1. Liver of No. 50. The figure shows the cut surface at right angles to the peritoneal surface.
- Fig. 2. Cut surface of the same liver enlarged two diameters to show the distribution of the yellowish zones along the course of the hepatic vessels.
- Fig. 3. Cut surface of healthy liver. The coloring is not properly reproduced in this figure.
- Fig. 4. Section parallel to the peritoneal surface of fresh liver from No. 106, in iodized serum. Slightly magnified. The yellow regions correspond to the regions in which the bile capillaries are distended with bile.

Fig 1

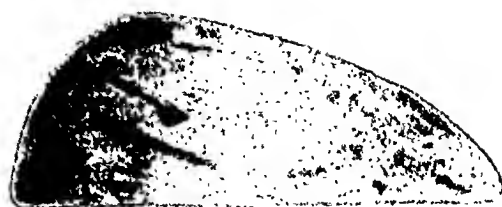


Fig. 2



Fig. 3



Fig 4

## PLATE III. BILE STASIS AND HAEMOGLOBINURIA.

Fig. 1. Section from liver of No. 130. Cut on freezing microtome, stained in alum earmine, floated upon the slide, dried in thermostat and mounted in xylol balsam. Drawn with Zeiss apochr. 4 mm. and compens. ocular 4. Outlined with camera lucida. ( $\times 250$ .) The hepatic cells are shown to be inclosed in a network of bile canaliculi distended with rods of solid bile. The space to the left represents the intralobular vein.

Fig. 2. From a fresh section of liver of No. 144, showing the network of injected bile canaliculi and the needle-like, red crystals.

Fig. 3. Rods of solid bile obtained from teased preparations of the liver of No. 184, ( $\times 1,000$ .)

Fig. 4. Urine from No. 80. (p. 302.)

Fig. 2



Fig. 4

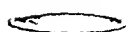


Fig. 3

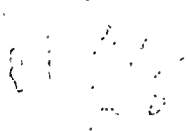


Fig. 1



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BILE STASIS AND HÆMOGLOBINURIA

## PLATE IV. MICROÖRGANISM OF TEXAS FEVER.

Fig. 1. Blood from a skin incision of No. 74, taken September 30, 1890. The blood was spread in a thin layer on a coverglass as described in the text, dried in the air. Subsequently heated for one to two hours in a dry hot-air oven at  $110^{\circ}$ – $120^{\circ}\text{C}$ . Stained for two to three minutes in Löffler's alkaline methylene blue, washed in water, then dipped for a moment in a one-third per cent solution of acetic acid, washed again, dried in the air, and finally mounted in xylol balsam. The microparasite is represented by the exceedingly minute blue points within the red corpuscles.

In this preparation the infection is shown to be very extensive. This is the only case in which the parasite was detected in this exceedingly minute stage. ( $\times 1,000$ .)

Fig. 2. Cover-glass preparation of spleen pulp from No. 70. Stained as described in Fig. 1 above. The intraglobular bodies are slightly larger than those of Fig. 1. ( $\times 900$ .)

Fig. 3. Blood from a skin incision of No. 160. Prepared November 7, 1891. Method as described. The small bodies are situated within the red corpuscles near the periphery. The large red corpuscle in the center containing a number of stained particles of different sizes is a result of the loss of corpuscles, or anaemia. ( $\times 1,000$ .)

Fig. 4. Cover-glass preparation from kidney of No. 130. Method of fixing and staining as described above. The large, blue body in the center of the group is one of the cellular elements of the kidney. The parasites are usually in pairs, and roundish. The form is generally assumed in the dead body. ( $\times 1,000$ .)

Fig. 5. Preparation made by rubbing a piece of the heart muscle of No. 186 on a cover-glass, drying and staining as before. In this way the blood corpuscles from the smaller vessels and capillaries are obtained. The large blue body represents a leucocyte. The parasites are mostly in pairs and pear-shaped. ( $\times 1,000$ .)



## PLATE V.

- Fig. 1. Cover-glass preparation of spleen pulp from No. 66. The two large blue bodies represent cell elements of the spleen pulp, and the uniformly bluish-pink body represents an "anaemic" red corpuscle. The red corpuscles are mostly larger than normal, owing to the anaemic condition induced in the animal before death. Many parasites are in pairs and have assumed the spherical form. The animal had died in the night. ( $\times 1,000$ .)
- Fig. 2. Preparation made as before from blood taken from a skin incision of No. 106, August 27, 1890, less than twenty hours before death. The appearance of the infected corpuscles in groups, as shown in the figure, was especially marked in this animal. The parasites are mainly in pairs, and pyriform. The stained body on the right is a white corpuscle. The large parasite in a corpuscle to the left was drawn in from an adjacent field. The reddish color of the stained bodies is due to the fact that the preparation was drawn while still mounted in water, which partly dissolved out the coloring matter. ( $\times 1,000$ .)
- Fig. 3. Cover-glass preparation of blood taken from a skin incision of No. 185, October 9, 1891. (Case of intravenous injection of Texas-fever blood.) On this date only about 1,000,000 red corpuscles in a mm. All objects within the dotted line are in one field of the microscope. The rest are drawn in from other fields in the same preparation; *a* represents modified red corpuscles, *b* a leucocyte, *c* a haematoblast, and *d* the parasites. Note the variation in the size of the red corpuscles. The parasites are mainly in pairs. They vary in size and form, and perhaps represent stages of degeneration. ( $\times 1,000$ .)

Fig 1



Fig 2

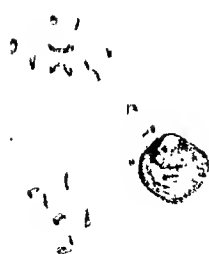
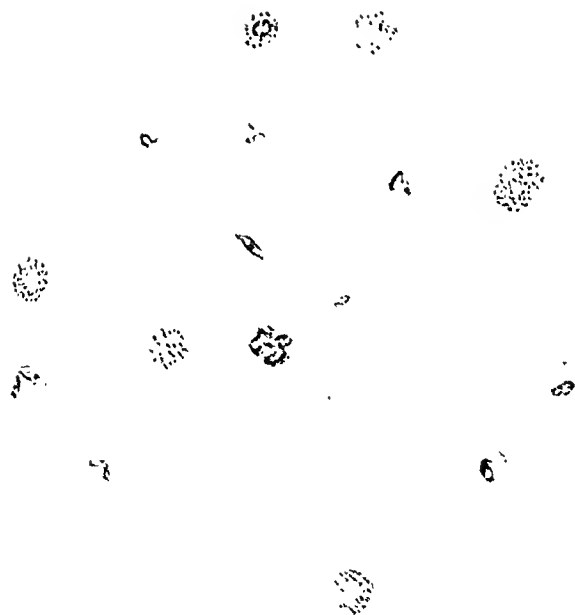


Fig 3



Homes, del

MICRO-ORGANISM WITHIN THE RED BLOOD CORPUSCLES.



## PLATE VI. MICROÖRGANISM OF TEXAS FEVER.

- Fig. 1. Vascular fringes on omentum of No. 130, crushed on cover-glass. Dried and stained as before ( $\times 1,000$ ). Shows the extensive infection of blood corpuscles in the capillaries. The large blue body represents a cellular element. One corpuscle shows a double infection. The parasites are mainly pyriform.
- Fig. 2. Heart muscle of No. 130, crushed on cover-glass, dried and stained to show presence of parasites freed by the disintegration of the infected corpuscles. One corpuscle in the lower part of the figure to the right shows faintly. The two pairs of free parasites above are drawn in from another field.
- Fig. 3. Preparation from kidney of No. 74, showing the large number of freed parasites in addition to an extensive infection of the red corpuscles. The free bodies largely in pairs.
- (p. 303)
- Fig. 4. Infected corpuscle, unstained, from cutaneous blood of No. 56, collected November 28, 1890. Each pyriform body is provided with a minute dark body not seen in stained preparations. ( $\times 1,000$ .)
- Fig. 5. A similar pair of parasites, unstained, from No. 130. Taken December 30, 1890. ( $\times 1,000$ .)
- Fig. 6. A spherical form from the same case at the same time.
- Fig. 7. Stained corpuscle from cutaneous blood of No. 137, prepared November 6, 1890, shortly before it was killed, showing how large these bodies may occasionally become with reference to the enveloping corpuscle. Note also the peripheral stain.
- Fig. 8. Free parasites not infrequently observed in crushed, fresh, and unstained preparations from the heart muscle of various cases. They are seen usually in pairs.
- Fig. 9. A series of corpuscles containing bright motile bodies, observed both in health and disease. Somewhat coarsely outlined.
- Fig. 10. Path of one of the bright motile bodies within a red corpuscle, as observed during a period of 15 minutes. Sketched from a fresh preparation of cutaneous blood from No. 107, August 25, 1890.

PLATE VI

Fig. 1



Fig. 2

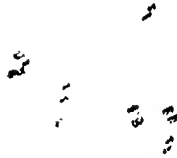


Fig. 4

Fig. 5

Fig. 3



Fig. 6

Fig. 7



Fig. 10



Fig. 8

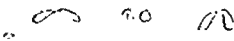


Fig. 9



Homes, del

MICRO-ORGANISM OF TEXAS FEVER.

## PLATE VII.

- Fig. 1. Capillary from heart muscle of No. 181. From tissue hardened in Müller's fluid and alcohol. Sections cut after imbedding in paraffin and fastened to the slide with a few drops of 70 per cent alcohol. Stained for an hour in Ehrlich's acid hematoxylin and eosin, dehydrated in alcohol containing eosin, cleared in clove oil, and mounted in xylol balsam. There are a considerable number of parasites in pairs within the red corpuscles, the majority of which show only in outline, since they have lost their coloring matter, probably as a result of disintegration. ( $\times 500$ .)
- Fig. 2. Capillary from the medullary portion of kidney of No. 186. Nearly every corpuscle contains a pair of parasites. Those drawn in shadow below the optical section in focus are also infected. The section was prepared in the same manner as detailed above, with the exception that it was not fastened to the cover glass and not passed through eosin alcohol. ( $\times 500$ .)
- Fig. 3. Capillary containing infected corpuscles almost exclusively. From a teased preparation of fresh spleen pulp of No. 134, in iodized serum. The unstained parasites appear as minute round white spots in the corpuscles. ( $\times 500$ .)

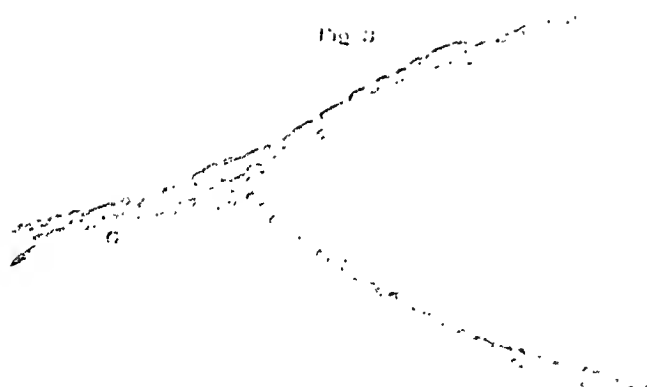
Fig 1



Fig 2



Fig 3



Homes, del

CAPILLARIES FILLED WITH INFECTED CORPUSCLES

## PLATE VIII. AMOEBOID CHANGES OF THE MICROÖRGANISM OF TEXAS FEVER.

Fig. 1. Fresh preparation of blood from No. 69, five hours post-mortem. Preparation sealed with paraffin and kept in a warm chamber with microscope at  $35^{\circ}$ - $40^{\circ}$ C. Showing changes of form in an intraglobular parasite.

Nos. 1 to 6, changes going on as fast as could be sketched.

Nos. 7 to 15, sketched twenty minutes later.

Fig. 2. An intraglobular parasite in subcutaneous blood of No. 95 a few hours before death, showing changes of outline.

Fig. 3. Another parasite from the same source, showing similar changes.

Fig. 4. Parasite showing a nuclear (?) body from the same source.

Fig. 5. Similar parasites sketched from the fresh cutaneous blood of No. 90, shortly before death. Note the different forms and relative positions occupied by the intraglobular parasites, as well as the presence of the nuclear (?) body.

Fig. 1

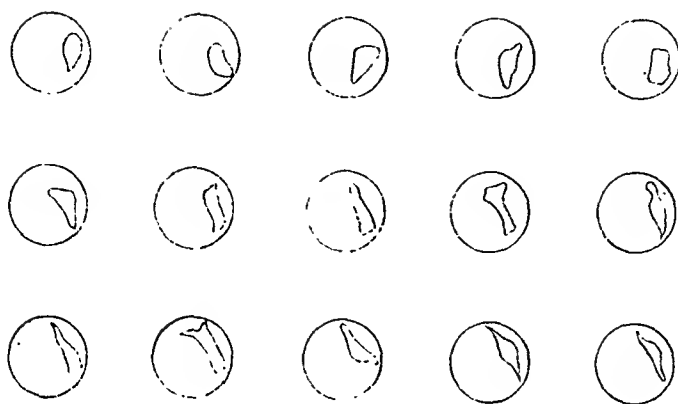


Fig. 2



Fig. 3

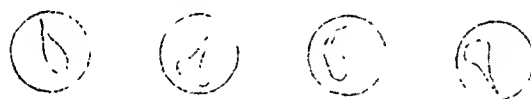


Fig. 4



Fig. 5



PLATE IX. MODIFIED OR EMBRYONIC RED CORPUSCLES AFTER SEVERE HEMORRHAGE AND AFTER TEXAS FEVER.

Fig. 1. Blood from sheep No. 160, upon which venesection had been practiced. Prepared July 7, 1890, after the number of red corpuscles had been reduced from eleven to five and one-half millions. Dried and stained as for Fig. 1 on Plate IV. Note variation in the size of the normal corpuscles and the presence of large corpuscles containing a large number of stained particles or granules of variable size. ( $\times 1,000$ .)

Fig. 2. Another field from the same preparation, showing also a tinted form without granules. ( $\times 1,000$ .)

Fig. 3. Cutaneous blood from cow No. 168, drawn August 12, 1891, after the red corpuscles had been reduced by venesection from six and one-half to two millions. Stained as indicated in Fig. 1. Note the presence of large and small granules in the corpuscles; also a uniformly stained corpuscle. ( $\times 1,000$ .)

Fig. 4. From another field of the same preparation, showing two large corpuscles containing stained granules. ( $\times 1,000$ .)

Fig. 5. Cutaneous blood from No. 160 (case of Texas fever). Preparation made November 12, 1891. A corpuscle on the left contains a Texas-fever parasite. ( $\times 1,000$ .)

(p. 304)

Fig. 6. Another field of the same preparation, showing uniformly stained as well as granular red corpuscles. Note also the great variation in size of the corpuscles having a normal appearance. ( $\times 1,000$ .)

PLATE IX

Fig. 1

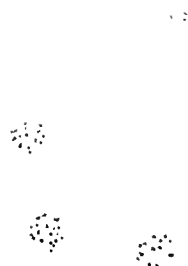


Fig. 2



Fig. 4

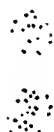


Fig. 3

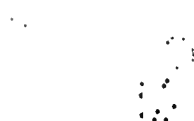


Fig. 5



Fig. 6





## PLATE X. THE CATTLE TICK—THE CARRIER OF TEXAS FEVER.

(Figs. 1, 3, 4, and 5 were drawn under the direction of Dr. Curtice. Nos. 4 and 5 were slightly modified before insertion.)

Fig. 1. A series of ticks from the smallest, just hatched from the egg to the matured female ready to lay eggs.

Fig. 2. Eggs magnified five diameters.

Fig. 3. The young tick just hatched. ( $\times 40$ .)

Fig. 4. The sexually mature male after the last moult. Dorsal view. ( $\times 10$ .)

Fig. 5. The sexually mature female after the last moult. Dorsal view. ( $\times 10$ .)

Fig. 6. A portion of the skin of the udder of No. 140. (Ticks artificially hatched and put on when small.)

Fig. 7. A portion of the ear of the same animal, showing adults ready to drop off and lay their eggs

Fig. 1

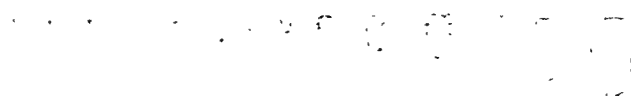


Fig. 2



Fig. 3

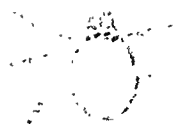


Fig. 4



Fig. 5

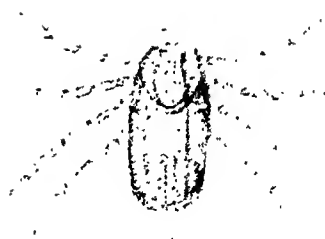
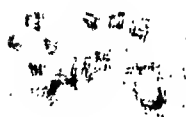


Fig. 6



Fig. 7






# A Comparative Study of Bovine Tubercle Bacilli and of Human Bacilli from Sputum

BY

THEOBALD SMITH, M.D.

*From the Laboratories of Comparative Pathology, Harvard Medical School, and the Massachusetts State Board of Health. Published in The Journal of Experimental Medicine, 3: 451-511, 1898*

HE absolute identity of tubercle bacilli infecting mammalia has been so generally assumed and the assumption used as a basis for the enactment of sanitary measures having for their object the prevention of any transmission of tubercle bacilli from animals to man, that any one who would attempt to question this identity must be prepared to meet considerable scepticism. Taking a broad biological position, we have every reason to examine into the assumed identity of the bovine and the human bacillus, because both the human and the bovine species are victims of a tuberculosis, presumably transmitted in most cases from one individual to another of the same species, and because the adaptation of a highly parasitic organism to one of these species for centuries may possibly deprive it of much of its power to multiply in the other. Or the reverse may be true. The adaptation of the bovine bacillus to a larger, more vigorous organization may thereby render it more dangerous to man. Assumptions of this sort stimulate inquiry but do not furnish us with positive information. This can be gained only by most tedious investigation.

In 1896 I presented to the Association of American Physicians\* a comparative study of a bovine bacillus and a presumably human bacillus which had passed from a tuberculous subject to an animal pet (*Nasua narica*, 'Coati'). The differences which appeared during this work were so clear, both as regards morphological

\* Trans. Assoc. Amer. Physicians, 11: 75-95, 1896.

and biological characters, that a further study was indicated. Imbued with the idea that in the minor, though constant, differences of closely related or apparently identical pathogenic bacteria many unexplained phenomena may (p. 452) have their source, and that a comparative study of tubercle bacilli under as nearly the same conditions as can be maintained may lead to results of value to human pathology, I took up the subject anew. A consultation of the literature treating of the character of tubercle bacilli had impressed me with the carelessness shown by most writers subsequent to Koch, concerning the source of the cultures used by them. Papers written on methods of cultivating the presumably human bacillus were really devoted to the avian bacillus. Fischel,† though drawing far-reaching conclusions on the relation of human to avian bacilli, makes no statement concerning his cultures save that they were "mammalian."

There being, therefore, no information to be gathered from former publications, the task that presented itself was to study a number of human and bovine tubercle bacilli, and, if possible, tubercle bacilli from other mammalia, side by side, in order to determine whether constant differences, of whatever nature, could be demonstrated. Such differential characters might then be applied in studying different forms of human tuberculosis, especially those cases which are supposed to have been derived from animals, more particularly from cow's milk.

The delay inseparable from the study of this disease has not permitted me to examine more than a limited number of cultures. Including the two described in 1896, 7 sputum and 6 bovine cultures have been isolated and studied; also one animal culture presumably derived from sputum, one culture each from the horse, the cat and the pig.

In Table I are given brief accounts of the subjects from which they were obtained. For the notes on the cases of phthisis I am indebted to a number of physicians who have very generously given their time in tracing the subsequent history.

(p. 456) It will be noticed that these cultures come from a variety of cases, both mild and severe. Of the patients yielding

† Fortschr. d. Med., 10: 908, 1892. See also my former article for further references.

TABLE I

Designation of culture	Beginning of artificial cultivation	Source of culture	History of case
Sputum I	July 20, 1896	Peabody, Mass.	Sputum discharged, June 24, 1896, by a young Irish woman. Apex and upper lobe of left lung involved. Slight fever. Sputum contains a considerable number of bacilli. Recovered and worked during summer. Good health in the fall of 1896, with gain in weight. Feb., 1898, in good health, works daily. No cough, expectoration or other symptoms of illness. Over the formerly involved region "the respiratory murmur much diminished down to 3rd rib. Increased vocal resonance, increased fremitus and dullness on percussion." Patient has moved from place to place.
Sputum II	Nov. 21, 1896	New Bedford, Mass.	Sputum containing many tubercle bacilli, discharged Oct., 1896, by a young man confined in prison about year. Earliest appearance of symptoms not accurately known. Slight cough noticed in Aug., 1896, but no definite physical signs at that time. Grew steadily worse, so that in November he was in bed, weak and emaciated and also suffering with diarrhea. He died in March, 1897.
Sputum III	Feb. 15, 1897	Norwood, Mass.	Sputum discharged, Jan. 12, 1897, by a man aged 45 years. Duration of disease about six months. Laryngeal tuberculosis chiefly. Difficulty in swallowing and huskiness of voice, which has been gradually increasing. Died Feb., 1897. The physician in charge had drawn off about a litre of serum from thorax 4 or more years ago. Well thereafter until fall of 1896. Apex of lungs slightly involved towards end of disease. Patient has traveled much in this country.

TABLE I—*Continued*

Designation of culture	Beginning of artificial cultivation	Source of culture	History of case
Sputum IV	Feb. 16, 1897	Melrose, Mass.	Sputum containing but relatively few bacilli, discharged Jan. 7, 1897, by a female servant, 22 years old. Physician in charge saw her first Dec., 1896. She complained of hoarseness and cough which began about 6 months ago. Signs of anemia and cessation of menstrual flow. Placed in hospital, where she remained 8 weeks. At end of April health quite re-established. A subsequent report mentions her visit to Canada after her recovery and her return to Massachusetts. She is now (Jan., 1898) at service in another town. She has a troublesome cough and is under the care of a physician. (p. 454)
Sputum V	July 7, 1897	New Hampshire	Sputum discharged, June, 1897, by a man 25 years old. Had been troubled with a cough for about 2 years, and apices reported involved. Patient feels well in the country, but cannot carry on his trade (printer) in the city. In Jan. 1898, he was reported to be much improved in every way.
Sputum VI	July 14, 1897	Winthrop, Mass.	Sputum discharged, June 16, 1897, by a woman 20 years old. Tubercle bacilli numerous. History not obtainable. Patient died about 6 months later.
Sputum VII	Jan. 18, 1898	Haverhill, Mass.	Sputum containing many bacilli, discharged by an Italian laborer, Dec. 15, 1897. Age of patient 27 years. Returned to Italy in Jan., 1898.

TABLE I—*Continued*

Designation of culture	Beginning of artificial cultivation	Source of culture	History of case
<i>Nasua narica</i> (Coati) human sputum?	July 26, 1894	Washington, D. C.	Autopsy, May 12, 1894, revealed primary intestinal infection, as mesenteric glands were farthest advanced in the disease. Omentum studded with tubercles. Extensive embolic tuberculosis of lungs. Household pet of tuberculous man. At Washington Zoological Park, where animal was kept after death of owner, other animals of same species remained well.
Bovine I	Dec. 1, 1894	Virginia.	Bull with advanced generalized disease. Great enlargement of lymph glands of head and thorax. Tuberculosis of the bones. Periodic tympanites due to enlarged mediastinal glands. Killed.
Bovine II	Nov. 28, 1896	Lawrence, Mass.	Cow having multiple necrotic foci in large caudal mediastinal gland. Foci dry cheesy; process evidently old. In one lobe of lung a focus $1\frac{1}{2}$ inches in diameter with center softened. In udder small nodules containing actinomycetes. Killed.
Bovine III	April 19, 1897	Carlisle (?), Mass.	Cow killed, March 19, 1897, at Brighton (Boston) abattoir. Quite extensive disease of lungs and liver. (p. 455)
Bovine IV	April 23, 1897	Billerica, Mass.	Cow killed, March 19, 1897, at Brighton abattoir. Disease restricted to one of dorsal mediastinal glands. The gland is moderately enlarged and contains a number of well-defined tubercles, 3 to 4 mm. in diameter, dry cheesy throughout, and easily peeled out of gland tissue. No surrounding infiltration. Evidently a mild stationary case.



TABLE I—*Concluded*

Designation of culture	Beginning of artificial cultivation	Source of culture	History of case
Bovine V	April 23, 1897	Carlisle, Mass.	Cow killed, March 19, 1897, at Brighton abattoir. Disease has produced a focus in the lungs, and involves all dorsal mediastinal glands, which are considerably enlarged. One of the portal glands is enlarged, and permeated with a net-work of necrotic lines.
Bovine VI	Dec. 24, 1897	Newton, Mass.	Caseous matter from a focus in the lungs of a cow 2 to 3 years old. The focus several inches in diameter, probably not more than 3 to 3½ months old, since the cow gave no tuberculin reaction 4 months ago. Dorsal mediastinal gland involved.
Swine I	May 8, 1896	Southboro, Mass.	Lungs and one gland (presumably from mesentery) received at laboratory, March 18, 1896. The herd lived under a cow stable, and the infection was probably bovine in origin. Lungs studded with firm, centrally cheesy or calcified nodules from 1 to 4 mm. in diameter. The lymph gland contained many foci with cheesy centres.
Cat I	Mar. 9, 1897		Case reported by L. Frothingham, V. M. D., in the Journal of the Boston Society of Medical Sciences, March, 1897. Tuberculosis of a mesenteric gland with miliary tuberculosis of lungs, liver and spleen. Tubercle bacilli in capillaries of lungs and liver. Guinea-pig inoculated by Dr. Frothingham, and kindly transferred to me.
Horse I	Feb. 20, 1897		Lungs of a horse from Brighton Rendering Establishment. Guinea-pig inoculated from tubercles by Dr. L. Frothingham. History of animal not known.

the sputum bacilli, three are dead, two still sick, one has apparently recovered, and one, a recent case, is now not accessible. Of the bovine cases two were slight, two advanced and two of moderate intensity. Of the other mammals nothing very definite is known.

The bacilli were isolated in all cases by inoculating guinea-pigs with tuberculous tissue or sputum containing bacilli. With sputum the injection of a suspension in bouillon into the abdominal cavity is the most satisfactory. Subcutaneous inoculation may induce a very chronic disease with older (500-gramme) guinea-pigs, which is not so likely to lead to successful cultures because of the scarcity of bacilli in the tuberculosis foci. In nearly all cases the guinea-pigs were chloroformed after three or four weeks, to prevent secondary infections occurring in the final stages of the disease.

Inasmuch as a more general study of tubercle bacilli is desirable, I shall go somewhat into detail concerning the methods I have employed in making cultures. Having had practically nothing but failures until I adopted the procedure to be described, I can recommend it without reserve. There is nothing new about it, excepting in the combination of details. Of 18 attempts to isolate the bacillus, 17 were successful. The one failure was probably due to the slow progress of the inoculation disease in the guinea-pig.

Throughout the work dog's serum was used. The dog was bled under chloroform and the blood drawn from a femoral artery, under aseptic conditions, through sterile tubes directly into sterile flasks. The serum was drawn from the clot with sterile pipettes and either distributed at once into tubes or else stored with 0.25 to 0.3 per cent chloroform added. Discontinuous sterilization was rendered unnecessary. The temperature required to produce a sufficiently firm and yet not too hard and dry serum is for the dog 75° to 76°C. For horse serum it is from 4° to 5° lower. The serum was set in a thermostat into which a large dish of water was always placed to forestall any abstraction of moisture from the serum. About three hours suffice for the coagulation. When serum containing chloroform is to be coagu-

lated, I am in the habit of placing the tubes for an hour or longer in a water-bath at  $55^{\circ}$ – $60^{\circ}$ C., or under the receiver of an air-pump, to drive off the antiseptic. This procedure (p. 457) dispenses with all sterilization excepting that going on during the coagulation of the serum. It prevents the gradual formation of membranes of salts, which, remaining on the surface during coagulation, form a film unsuited for bacteria. Tubes of coagulated serum should be kept in a cold closed space where the opportunities for evaporation are slight. They should always be kept inclined.

The ordinary cotton-plugged test tubes I do not use, because of the rapid drying out permitted by them, as well as the opportunities for infection with fungi. Instead, a tube is used which has a ground glass cap fitted over it. This cap contracts into a narrow tube plugged with glass wool. This plug is not disturbed. The tube is cleaned, filled and inoculated by removing the cap. With sufficient opportunity for the interchange of air very little evaporation takes place, and contamination of the culture is a very rare occurrence. In inoculating these tubes, bits of tissue, which include tuberculous foci, especially the most recent, are torn from the organs and transferred to the serum. Very little crushing, if any, is desirable or necessary. I think many failures are due to the often futile attempts to break up firm tubercles. Nor should the bits of tissue be rubbed into the surface, as is sometimes recommended. After a stay of several weeks in the thermostat I usually remove the tubes and stir about the bits of tissue. This frequently is the occasion for a prompt appearance of growth within a week, as it seems to put certain still microscopic colonies in or around the tissue into better condition for further development. The thermostat should be fairly constant, as urged by Koch in his classic monograph, but I look upon moisture as of more importance. If possible, a thermostat should be used which is opened only occasionally. Into this a large dish of water is placed, which keeps the space saturated. Ventilation should be restricted to a minimum. As a consequence, moulds grow luxuriantly and even the gummed labels must be replaced by pieces of stiff manila paper fastened to the tube with

a rubber band. By keeping the tubes inclined, no undue amount of condensation water can collect in the bottom, and the upper portion of the serum remains moist. The only precaution to be applied to prevent infection with moulds is to thoroughly flame the joint between tube and cap as well as the plugged end, before opening the tube. When test tubes are employed it is well to dip the lower end of the plug into sterile molten paraffine and to cover the tube with a sterilized paper cap. The white bottle caps of the druggists are very serviceable.

In pursuing this method of obtaining cultures, the question arises: May not attenuated or more saprophytic forms exist in the sputum (p. 458) besides those more pathogenic, and may not the former get into our cultures rather than the latter? This question cannot be answered with entire satisfaction. If we assume, for the sake of illustration, that the original disease was due to perhaps one inhaled bacillus, the progeny of this bacillus may be reinforced by others inhaled which have more saprophytic and less pathogenic tendencies, and which multiply in the cavities and in the sputum to the partial suppression of the original form. If we make cultures directly from sputum this hypothetical danger could not be evaded. The inoculation of the guinea-pig and the three or more weeks elapsing before cultures are made is to a certain degree a safe-guard, as it gives the more pathogenic form an opportunity to assert itself by prompt multiplication. I am not inclined to look upon this danger of substitution as a real one. At the same time, it may be best always to choose those successful cultures from the guinea-pig which have come from metastatic rather than local (peritoneal) tubercles. In my work I obtained in most cases cultures simultaneously from 3 or 4 organs, and any differences in these original cultures were not manifest. Only one was used in the comparative studies. Of 7 sputum cultures, 2 were derived from the omentum and 4 from the spleen. Of one the source is not noted. For the bovine cultures no such doubts can be raised, because the foci are closed and not accessible to more saprophytic types.

In the study of the various cultures the conditions were maintained as nearly uniform as possible by using tubes of serum

prepared at the same time, and keeping the inoculated cultures in the thermostat in the same trays. For the microscopic examination a little of the surface growth was rubbed between two cover glasses, allowed to dry in the air, and then the whole series to be compared were fixed all together in the hot-air sterilizer at 120°C. for 20 to 30 minutes. For staining, carbolfuchsin was used cold, and the decolorization effected with a 10 per cent aqueous solution of sulphuric acid acting for from 15 to 30 seconds. Coverslips were also decolorized with  $\frac{1}{2}$  per cent acetic acid, some simply washed in water, others were stained according to Gram-Weigert. In all cases the members of the series studied were treated alike and at the same time, thus eliminating minor, often unavoidable, variations. In all cases the characters to be described refer to dog-serum cultures. These were renewed every 3 to 6 weeks, as many at a time as was possible. The regularity of re-inoculations was now and then interrupted by a beginning infection of the tube with moulds, or a too feeble growth, necessitating (p. 459) earlier transfer to fresh tubes. As a rule the cultures were kept continuously in the thermostat until the next transfer was made.\*

The tendency of most species of bacteria to vary slightly from tube to tube, either in size, form, or staining capacity, is also characteristic of tubercle bacilli, so that repeated examination of series of cultures is necessary to obtain what might be called a composite photograph of their most permanent characters or peculiarities. The statements made below as to the morphology of the bacilli under observation are based on the repeated examination of hundreds of slides of which the conditions of growth of the bacilli, the coagulating point of the serum, and the staining manipulations had been carefully noted. The cultivation of tubercle bacilli requires, even under the best circumstances,

\* It is always desirable as a precautionary measure to retain 3 or 4 older transfers of any culture in a cool, dark place, so that it may not be lost through some accident or contamination. Now and then culture-media will prove unsatisfactory. In such cases, the earlier tubes must again be resorted to. I have noticed that upon all the serum tubes from one dog, growth was feeble. The liver and the kidneys of this animal showed considerable fatty changes, although the animal had not been ill. Possibly over-feeding may be the cause of the difficulty.

constant personal attention, and those not prepared to give it had better not attempt it seriously. Success is obtainable along lines other than those suggested by me. Koch succeeded by using beef's serum in ordinary plugged test tubes. He is, however, the only investigator, I believe, who has studied series of cultures of tubercle bacilli.

#### MORPHOLOGICAL AND BIOLOGICAL CHARACTERS

With one exception to be noted below (Sputum I), the human bacilli grew from the start much more vigorously than the bovine bacilli. With several the rapidity of growth was surprising. After two weeks these cultures appear as a whitish surface layer of a pearly lustre, of varying thickness. The bovine cultures show merely discrete colonies, or a thin, uniform layer having the appearance of ground glass.\* This difference in the vigor of growth has, in general, maintained itself, with the slowly increasing tendency of all cultures to multiply more rapidly.

The size of bovine bacilli in the various cultures was quite constant. They were all quite short, usually about 1 to 1.5  $\mu$  long, more rarely 1 (p. 460) to 2  $\mu$ . These measurements do not tend to change appreciably with prolonged cultivation. The bacilli are straight, not very regular in outline. Some are broader at one end than at the other, some broader in the middle than at either end, i.e. spindle-shaped. Some may be so short as to resemble oval cocci. With the human bacilli the form was not so constant. The earliest cultures of Sput. II, IV, V and VI contained forms from 1 to 2  $\mu$  long, hence closely approximating the bovine forms. Others (Sputum III) may be longer from the start. In all, however, there is a tendency, not noticed among bovine cultures, to grow longer under artificial cultivation. Perhaps the greatest contrast in form, which has remained so for three years, is illustrated by the bovine and the Nasua (human) culture described in 1896. In the latter the bacilli are from 2 to 3 times the length of the former.

\* In some tubes a peculiar coppery discoloration may extend over the entire surface growth. Cultures from these are fertile, however. There is nothing in the microscopic appearance of the bacilli to explain this change. It is not an uncommon feature of cultures of feeble vitality, or of unsatisfactory culture-media.

In the earliest cultures, therefore, morphological differences are not necessarily characteristic, and cannot aid us in attempts at determining the origin of cultures. Cultures containing only small forms have been noted by Metchnikoff and Straus. The latter states that even the avian variety may assume very small dimensions under certain circumstances.

When the serum to be used for cultures is coagulated at a temperature of  $71^{\circ}$  to  $72^{\circ}\text{C.}$ , instead of  $75^{\circ}$  to  $76^{\circ}\text{C.}$ , certain modifications are manifest. All bacilli which have developed on a serum having a firm surface, and which is obtained at the higher temperature, absorb the dye promptly and become brilliantly stained. When a softer ( $71^{\circ}\text{C.}$ ) serum is employed, whose surface is easily depressed, torn and broken by the platinum needle, the culture, which may have become either more or less vigorous than before, now contains a large number (from 50 to 90 per cent) of bacilli, which stain quite feebly. Uniformly dispersed among them are deeply stained forms. This feeble stain is noticed when bacilli are not treated with decolorizing agents at all, and the appearance of the cover-slip preparation is not materially altered by the acid.\*

While both human and bovine bacilli are affected by the softer serum, the former show a much greater degree of change. The bacilli are very feebly stained and show outlines often very indistinct. Further than (p. 461) this, the human bacilli, on the softer serum, tend to become longer and slightly curved. In some cultures this change is very pronounced, in others less so. With the bovine forms there is no elongation, although the bacilli may be less brilliantly stained than on firm serum. Of seven human cultures studied, all have exhibited this tendency to become slender, while none of the bovine bacilli have been seen to change their size to any appreciable degree. Some of the bo-

\* Since the completion of the manuscript further studies of this phenomenon have convinced me that at least some of the feeble staining is due to the formation of a capsular substance, which interferes with the penetration of the dye. This substance, which is produced in greatest abundance by the human cultures, is not infrequently detected as an irregular, unstained envelope around a single bacillus or a group. It is not stained by the procedure recommended by Prof. Welch for staining capsules.

vine cultures from softer serum did not even show any feebly stained bacilli.

Another modification in form which manifests itself upon the firmer serum is the appearance of round, deeply stained bodies, at or near the end of the usually slender bacilli, very rarely in the middle. These bodies, from 1.5 to 2 times the diameter of the rod, take a brilliant stain in carbol-fuchsin, contrasting with the more feebly stained, less compact rod in which they are imbedded. These bodies, which have a striking resemblance to spores, may be present in all the rods of any one preparation, or in a certain proportion only. They have been seen in Nasua, Sputum III, IV and VI. In the bovine cultures bodies of this nature are occasionally recognizable, but owing to the shortness of the bacilli they do not stand out distinctly. Of much more frequent occurrence in these cultures, often the only forms present, are short fusiform or spindle-shaped rods, the central swelling being also deeply stained, and perhaps corresponding to the terminal body of the human forms. These bodies have been seen by Ehrlich, Nocard and Roux, Metchnikoff, Cornil and Babes, Czaplewski and Straus. They have been variously interpreted as spores, and bacilli containing them have been successfully double-stained. Their significance remains unsolved. The most probable explanation is a degeneration or involution form. They may, however, represent some resting stage and correspond to the short, brilliantly stained bodies frequently seen in giant cells, and not recognizable as bacilli. In unstained films, mounted in water, they cannot be distinguished even with a very narrow pencil of light. An increased refrangibility cannot be made out.

Experiments to determine the length of time required at 60°C. to destroy both human and bovine forms have thus far not revealed any differences. The tests are reserved for a special publication.

A study of the relative resistance of the bacilli to drying has not yet been attempted.

Among the sputum cultures is one (No. 1) which grew so feebly on dog's serum that its cultivation was finally given up. The history of the case is briefly given in Table I. Since the com-



parative tests of the pathogenesis of this culture are very incomplete, I shall give briefly the (p. 461) results of the inoculation of the sputum as evidence that the organism was in reality a tubercle bacillus.

June 27, 1896. Guinea-pig, weight 640 grammes, receives into abdomen 0.5 cc. of bouillon in which some sputum is suspended.

July 20. Weight 457 grammes. Animal rather dull, with coat slightly staring. Very little resistance to handling. Chloroformed.

A few subserous tubercles around point of injection. Omentum represented by a cylindrical mass of neoplastic tissue, about 1 to 2 cm. in diameter, firm, speckled with whitish dots indicative of necrosis. Tubercles on diaphragm and testicles. Liver spotted with small, irregular, not well-defined, yellowish necroses. Spleen slightly enlarged, with Malpighian bodies prominent. Bronchial and sternal glands enlarged, with central necrosis. Lungs free from visible tubercles.

The pathogenic power of this sputum seems to have been equal to that of most sputa examined. One guinea-pig of 672 grammes, inoculated precisely like the preceding, died 46 days after inoculation, with more pronounced lesions of the liver and spleen. A third guinea-pig of 370 grammes, which had received the same quantity subcutaneously, weighed a trifle more on the 49th day (390 grammes) than at the beginning. On this day it was chloroformed and examined. The typical ulcer with surrounding tubercles in the subcutis and a few tubercles in the omentum were seen. The liver was pale and fatty, the spleen enlarged to several times the normal size and uniformly permeated with grayish (one mm.) foci, but without necroses. The lungs were studded with small, partly necrotic tubercles. The bronchial and sternal glands were large, with necrotic centres.

The first culture showed somewhat slender but well-stained bacilli. In tubes subsequently inoculated, the bacilli multiplied almost exclusively in the condensation water, which became milky in appearance. In this the bacilli appeared in roundish clumps among cholesterin crystals. The bacilli were imbedded in a colorless material which formed the cohesive clump. The stained bacilli presented no unusual characters save in one culture (after about six months of total cultivation), in which fully one-half of

all the quite slender bacilli appeared as series of transverse, apparently unconnected stained blocks, simulating streptococci. It is unfortunate that more animal tests were not made with this stock. As I was expecting a more vigorous culture from month to month, tests were postponed until conditions should approximate those of the other cultures. These were, however, not realized. The only test upon a rabbit is given in Table III. The cultivation was finally abandoned.

(p. 463) Of the other animal bacilli the cultures from swine were identical with the bovine cultures in morphological and other characters. Those of the horse and the cat were also either identical with the bovine bacilli or they very closely resembled them.

If we undertake to summarize the observations made with microscope and culture tube upon these bacilli, we somewhat hesitatingly formulate the following general statements:

1. Bovine and other animal bacilli (except *Nasua*, which is regarded as coming from man) grew less vigorously for a number of generations than the sputum bacilli. Sputum I is an exception and is probably an atypical form.
2. Bovine bacilli are much less influenced by certain modifications of the culture-medium.
3. Bovine bacilli tend to remain short; human bacilli are either more slender from the start or become so during cultivation.

#### PATHOGENESIS

The most important means of demonstrating identity or divergence of characters of pathogenic bacteria is the test upon animals. This test is a purely physiological one, but in the application of experimental results from the domain of bacteriology to medicine, morphological characters must give way to physiological.

That there might be differences among tubercle bacilli from different species of mammals presented itself as a possibility to Koch and is referred to in his monograph. He, however, failed to recognize any differences worth mentioning. There are several reasons for this. In the first place, Koch was at that time en-

deavoring to prove to the world that the tubercle bacillus is the cause of tuberculosis. Minor details received no attention because of the great and difficult task immediately before him. In the second place, the course of tuberculosis is essentially a function of the number of bacilli introduced. Variations in the dose result in corresponding variations in the length of the disease, in its final termination, and in the extent and distribution of the lesions. This fact Koch himself recognized in discussing the results following the intra-ocular inoculation of varying quantities of culture material in rabbits. He did not, however, attempt to adjust (p. 464) carefully the quantity to be injected or to determine the effect of varying quantities of bacilli upon any of the species used by him. Curiously enough, no one following him seems to have considered it worth while to extend his work by more accurate comparative tests. That such work is likely to be fruitful the following experiments amply demonstrate.

*Guinea-pigs.*—The inoculation of this species with tubercle bacilli from the various cultures brought out few well-defined differences. The great susceptibility of guinea-pigs to tubercle bacilli is responsible for the general acceptance of a common level of pathogenic power for all mammalian tubercle bacilli. This tendency to unify physiological characters because of a more or less uniform action upon very susceptible species has led to frequent failure on the part of experimenters to recognize important variations among species of bacteria, variations probably having much influence upon the course of the disease contracted in the natural way. There are, however, certain differences in the action of bovine and sputum bacilli upon guinea-pigs which enable us to recognize even in these very susceptible animals the much greater virulence of bovine bacilli. It is probable that by a graded dosage of tubercle bacilli more marked differences might be brought out than I am in position to present.

It has already been stated that all the cultures in hand had been obtained by inoculating the tuberculous tissue or the sputum into guinea-pigs and isolating the bacilli from them. To obtain the bovine cultures, a small bit of tissue was placed in a subcutaneous pocket in the flank. For sputum bacilli the spu-

tum was shaken up in sterile bouillon and the dilution injected into the abdominal cavity. In these preliminary experiments differences presented themselves between the two kinds of material. Although the sputum, as a rule, contained very many tubercle bacilli and the bovine tissue very few, yet the subcutaneous injection of sputum led to such a chronic disease, with comparatively slight lesions and a tendency to reparative changes in the liver, that the animals were very unpromising subjects for culture when chloroformed.\* Hence the intra-abdominal inoculation in most cases. On the other hand, the disease due to bovine tissue placed in the subcutis never failed (p. 465) to produce extensive lesions, with indications of certain death in 4 to 6 weeks, which was anticipated by chloroform when cultures were to be made. Leaving this preliminary series of inoculations, we will pass to those made with definite doses of tubercle bacilli in suspension.

The suspension was made by thoroughly rubbing the growth from blood serum upon the inside of dry sterile test tubes with a heavy spatula-like platinum wire. This procedure results in the breaking up of clumps and the coating of the tube with masses of bacilli. Bouillon was then poured in and the thoroughly stirred suspension allowed to stand for several hours until all coarser particles had subsided. The resulting suspension was diluted, if necessary, until its density was nearly equivalent to that of a bouillon culture of typhoid bacilli 20 to 24 hours old, and nearly as homogeneous. More accurate dosage might be obtainable by weighing the moist growth before suspending it in bouillon; but inasmuch as the weighed quantity may not all be brought into a finely divided state—a matter of importance in the intravenous injection of rabbits—the method adopted is probably less troublesome and equally accurate.

Of this suspension the usual dose, both for subcutaneous and intra-abdominal inoculation, was 0.5 cc. An examination of the dates in the various tables will show that many of the inoculations upon rabbits, guinea-pigs and cattle were made with the same suspension on the same day.

\* These statements apply only to guinea-pigs weighing 400 grammes and above.

The guinea-pigs employed were all rather large, weighing, with few exceptions, from 400 to 700 grms. They had all been used in diphtheria antitoxin tests one to three months before. The rapid increase in weight was evidence of no disturbance of health at the time of inoculation. It is of importance to bear in mind that the animals were large, because, the progress of tuberculosis differs essentially in growing and adult guinea-pigs, the latter manifesting a far greater resistance than the former, a resistance expressed by well-marked reparative or cirrhotic changes in the liver. The differences to be pointed out in the bovine and sputum series may possibly be nearly wiped out by the use of guinea-pigs weighing only 250 to 300 grms.

The disease induced by the intra-abdominal injection was so rapid in its progress for both bovine and sputum cultures that the virulence of both races appears nearly the same.

The shortest period between inoculation and death, when 0.5 cc. of the suspension was injected, is 7 days, the longest 21 days, with one (p. 466) exception, that of Sputum VI, which was 38 days. In other cases the period was prolonged because of smaller doses. For Bovine I (0.2 cc.) it was 33 days; for Nasua (0.3 cc.) 41 days. If we take the largest series in which the injections were made at the same time and in which the conditions were identical—the series comprising cultures of Sput. IV, V, VI, and of Bovine III, IV, V—we find the periods elapsing between inoculation and death to be respectively 21, 11, 38 for the sputum and 7, 9 and 10 days for the bovine cultures.

The disease due to the intra-abdominal injection of tubercle bacilli in the quantity used is peculiar in this, that there is always found after death a large quantity of an opalescent fluid in both pleural sacs. This fluid greatly compresses the lungs and is probably the immediate cause of death. When the disease is prolonged beyond 3 weeks, the pleural effusion is absent. A careful histological study of the various organs in this most acute form of the inoculation disease, which will probably furnish the explanation of the effusion, is still to be made. In the abdominal cavity there is, as might be expected, a general inflammation of the peritoneum associated with some fibrinous exudation and

usually a little viscid fluid, when the disease does not last quite ten days. Any prolongation beyond this brings a dense eruption of tubercles into view. The omentum is in all cases represented by a cylindrical mass of fused tubercles.

If we turn to the subcutaneous inoculations, the difference in pathogenic power is more clearly brought out.

In the same series just quoted, of the three sputum guinea-pigs, one died 44 days after inoculation, the others were chloroformed respectively 77 and 100 days after inoculation; the first having lost but little in weight, the second being a trifle heavier, but having extensive pulmonary disease. The bovine guinea-pigs died in 51, 41 and 40 days respectively. The sputum guinea-pig, which succumbed in 44 days, weighed at the start 130 grms. less than the lightest bovine guinea-pig. The lesions were slight, the lymph glands only moderately enlarged, the foci in the lungs not visible to the naked eye. The spleen was not enlarged. The liver was mottled with very many grayish specks. The microscopic examination showed lesions but slightly advanced and reparative changes with proliferation of bile-ducts in progress. In general, the tuberculous lesions in this animal did not warrant so early a death.

The histological examination of the tissues of the infected guinea-pigs was restricted to the lungs and the liver of those inoculated simultaneously (p. 467) under the skin with cultures of Sputum IV, V, VI,\* and of Bovine III and V. These organs were chosen because of their peculiar behavior towards the infection. The liver is invaded first, and under favorable conditions cirrhotic changes may begin which in some cases apparently lead to an elimination of the disease, with considerable shrinking of the organ and furrowing of the surface. In the lungs the disease begins later, and if the animal survives the first 6 weeks, may grow steadily until most of the organ is involved.

Pieces of tissue hardened in Zenker's fluid or alcohol were cut embedded in paraffine. The sections, fastened to the slide with Mayer's albumen and water combined, were stained with haemalum and eosin or picro-acid-fuchsin, or with eosin and methylene-

\* Spleen in place of liver in this case, the latter having been rejected by mistake.

blue. In some cases Weigert's fibrin stain was resorted to. All were stained for tubercle bacilli, in carbol-fuchsin, differentiated in 1 per cent acetic or decolorized in 4 per cent sulphuric acid, and stained subsequently in Löffler's methylene-blue. The stain for tubercle bacilli was successful in the tissues hardened in Zenker's fluid. Even in the sections stained according to Gram-Weigert, the bacilli appeared distinctly, but in a peculiar form, often simulating short streptococci with the individual cells rather well separated, or series of short blocks with space between them. Here the stain fastens itself only upon certain segments of the bacillus, leaving the connecting elements entirely unstained. The part selected evidently stands in no relation to the bulging, deeply stained, spore-like bodies referred to above as occurring in cultures.

In discussing the histological changes induced by tubercle bacilli in the various animals inoculated, it has been my determination to steer clear of all controversial questions relating to the histogenesis of the tubercle or of the elements composing it, as being foreign to the scope of this etiological study. Only those features will be very briefly referred to which show pronounced variations and which serve to point out differences in the action of the bacilli.

In the liver of the inoculated guinea-pig, the proliferative lesions present in all cases examined consist of aggregations of the characteristic epithelioid cells, among which, here and there, scattering nuclei appear richer in chromatin, and which for convenience are designated lymphoid elements. The lesions, situated chiefly in the interlobular tissue, are surrounded with a wide or narrow zone of proliferating bile-ducts, which appear as single or forked lines or in the form of meshes. There is nothing (p. 468) in the microscopic appearance of the liver tubercles to serve as distinguishing marks, excepting the much more extensive involvement of the liver tissue and the much greater abundance of tubercle bacilli in the bovine cases. In the latter there are added to these lesions those of another character, the simple necrosis of cell territories ushered in by a fading out of the nuclei and a deep stain with eosin. These areas probably represent the

yellow cheesy areas so common, and often very large, in young tuberculous guinea-pigs. They are readily distinguishable with the naked eye from the grayish proliferative changes going on in the interlobular tissue. In the sputum cases the very rare areas of this character seen were very small.

In the lungs, the lesions are as a rule perivascular and peribronchial. There are no essentially distinctive features here, excepting the very great abundance of tubercle bacilli in the bovine cases. In Bov. III the bacilli are also found in large numbers in cell detritus occupying alveoli and small bronchi. In Sputum VI many alveoli in the periphery of the foci are nearly filled out with multinucleated cells resembling giant cells closely, but their contents are only pigment particles. In Bovine V similar cells are present, though in small numbers. These, as well as other cells in the alveoli, each contain several bacilli.

The action of tubercle bacilli from the pig, the horse and the cat upon guinea-pigs was nearly the same as that of the bovine cultures, and needs no special discussion here.

With this hasty, imperfect sketch we may conclude the notes on the tuberculosis of guinea-pigs induced with cultures, by simply adding that the bovine bacilli studied are more virulent than human bacilli, although, owing to the great susceptibility of this species, the differences are not likely to impress us unless we give much attention to experimental details. These differences may be summed up as consisting in the more rapid death of all guinea-pigs inoculated with bovine bacilli, the greater extent of the lesions and the far greater abundance of tubercle bacilli in them.

In Table II will be found, in part, the basis for these conclusions.

(p. 470) *Rabbits*.—The inoculation into the anterior chamber of the eye has been the most widely practised method. This seems to have been followed by variable results, whether due to the number of bacilli injected, the source of the bacilli or the amount of injury inflicted on the eye.

Koch injected tubercle bacilli from various sources into an ear-vein. The bacilli were suspended in blood-serum and the sus-



TABLE II  
*Guinea-pigs*

Culture	Total age of artificial culture	Num-ber of trans-fer	Date of inoculation	Age of culture used, in days	Dose in cc.	Mode of inoculation	Initial weight in grammes	Final weight	Result
Sputum I	No inoculation of cultures.		(Of sputum suspension)		0.5	intra-abd.	672	430	Dies Aug. 11-12.
" II	{ 3 mos. 3 days.	5th	June 27, 96. Feb. 24, 97.	24	0.5 { 0.5	sub-cut. intra-abd. sub-cut. intra-abd.	370 640 570 600	390 457 520	Chloroformed August 15 (active). " July 20 (sick). Chloroformed April 19. Dies March 6-7 (10-11 days).
" III	{ 5 " 10 "	8th	May 1, 97.	9	0.5	" "	440	312	" May 13 (13 days).
" IV	{ 1 " 19 "	2d	April 3, 97.	18	0.5	" "	525		" April 12-13 (9 days).
" V	{ 2 " 17 "	4th	May 1, 97.	9	0.5	" "	435	245	" May 17 (17 days).
" VI	{ 2 " 16 "	2d	May 1, 97.	18	0.5	" "	705		" May 15-16 (15 days).
" VII	{ 6 " 10 "	7th	Aug. 26, 97.	9	0.5	sub-cut.	372	275	" Oct. 9.
" VIII	{ 6 " 10 "	7th	Aug. 26, 97.	9	0.5	intra-abd.	507		" Sept. 16-17 (21 days).
" IX	{ 1 " 19 "	3d	Aug. 26, 97.	9	0.5	sub-cut.	458	402	Chloroformed Dec. 3.
" X	{ 1 " 12 "	3d	Aug. 26, 97.	9	0.5	intra-abd.	517		Dies Sept. 5-6 (11 days).
" XI	{ 1 " 10 "	3d	Aug. 26, 97.	9	0.5	sub-cut.	420	431	Chloroformed Nov. 11, extensive lung disease.
" XII	{ 1 " 10 "	2d	March 1, 98.	16	0.5	intra-abd.	478	338	Dies Oct. 3 (38 days).
" XIII	{ 1 " 10 "	2d	March 1, 98.	16	0.5*	sub-cut.	323	360	Dies May 14-15.
" XIV	{ 1 " 10 "	2d	March 1, 98.	16	0.5*	intra-abd.	332	222	Dies March 18-19 (18 days).
" XV	{ 1 " 10 "	2d	March 1, 98.	16	0.5	sub-cut.	405	?	Chloroformed May 14 (failing).
" XVI	{ 2 " 27 "	3d	Feb. 24, 97.	24	0.2	intra-abd.	478		Dies April 22 (33 days).
" XVII	{ 2 " 27 "	3d	Feb. 24, 97.	24	0.5	sub-cut.	580	?	" Mar. 24
" XVIII	{ 5 " 3 "	5th	May 1, 97.	9	0.5	intra-abd.	645	?	" Mar. 3-4 (7 days).
" XIX	{ 5 " 3 "	5th	May 1, 97.	9	0.5	" "	505	?	" May 13 (13 days).

Bovine III	{ 4 mos. 7 days. 9 " 27 " 4 " 3 " 4 " 3 " 2 " 18 " 19 " 22 "	5th	Aug. 26, 97.	9	{ 0.5 0.5 0.5 0.5 0.5 0.5* 0.5* 0.75	sub-cut. intra-abd. " " sub-cut. intra-abd. sub-cut. intra-abd. sub-cut.	533 624 581 635 533 504 490 406 423 455	400 ? 468 400 ? 336	Dies Oct. 17-18. " Sept. 2-3 (7 days). " Mar. 2 (15 days). " Oct. 6-7. " Sept. 4-5 (9 days). " Oct. 5. " Sept. 5-6 (10 days). Dies May 2-3. Dies April 7 (23 days). " April 26, probably chronic kidney disease.
Nasua		18th	Mar. 20, 96.	16	{ 0.3 0.5 1.0 0.5 0.5 0.75 0.75 0.5	intra-abd. sub-cut. intra-abd. " " sub-cut. intra-abd. sub-cut. intra-abd.	505 525 525 450 395 415 424 427	? ? ? 300 290 290 ?	Dies May 1 (41 days). " Aug. 7. " July 25-26. " May 15 (14 days). " Aug. 19-20. " Aug. 7 (14 days). " Aug. 28-29. " Aug. 8 (15 days).
Swine I		14th	July 14, 96.	12	{ 0.3 0.5 1.0 0.5 0.5 0.75 0.75 0.5	intra-abd. sub-cut. intra-abd. " " sub-cut. intra-abd. sub-cut. intra-abd.	505 525 525 450 395 415 424 427	? ? ? 300 290 290 ?	Dies May 1 (41 days). " Aug. 7. " July 25-26. " May 15 (14 days). " Aug. 19-20. " Aug. 7 (14 days). " Aug. 28-29. " Aug. 8 (15 days).
Horse I		16th	May 1, 97.	13	{ 0.3 0.5 1.0 0.5 0.5 0.75 0.75 0.5	intra-abd. sub-cut. intra-abd. " " sub-cut. intra-abd. sub-cut. intra-abd.	505 525 525 450 395 415 424 427	? ? ? 300 290 290 ?	Dies May 1 (41 days). " Aug. 7. " July 25-26. " May 15 (14 days). " Aug. 19-20. " Aug. 7 (14 days). " Aug. 28-29. " Aug. 8 (15 days).
Cat I		5th	July 24, 97.	18	{ 0.3 0.5 1.0 0.5 0.5 0.75 0.75 0.5	intra-abd. sub-cut. intra-abd. " " sub-cut. intra-abd. sub-cut. intra-abd.	505 525 525 450 395 415 424 427	? ? ? 300 290 290 ?	Dies May 1 (41 days). " Aug. 7. " July 25-26. " May 15 (14 days). " Aug. 19-20. " Aug. 7 (14 days). " Aug. 28-29. " Aug. 8 (15 days).

\* Dilution one-third to one-fourth of that hitherto used.

pension passed through fine gauze to eliminate coarser particles. 4 rabbits were inoculated in this way with bacilli from a monkey, 3 with bacilli from a case of phthisis and 3 with bacilli from cattle. The rabbits all succumbed in from 18 to 31 days, excepting one, which was killed on the 38th day. In another experiment a culture from a case of lupus and from a monkey were tested on rabbits. Death ensued in 2 to 3 weeks. The weight of the rabbits and the density of the suspensions used are not given, so that comparisons are impossible. Moreover, the medium used—liquid serum—may not be entirely indifferent. Straus\* mentions the slight effect produced upon rabbits by cultures of human tubercle bacilli.

In the present work, the injection of tubercle bacilli into an ear-vein was used at first tentatively, then, when sharp distinctions between bovine and human cultures were made manifest by this procedure, it was continued.

Rabbits weighing from 1300 to 2200 grams were employed. The suspension was prepared as already described, and for most of the primary tests 0.5 cc. was injected. By referring to Table III it will be seen that for the primary test of the last pair of cultures, Bovine VI and Sputum VII, the suspensions were  $\frac{1}{3}$  to  $\frac{1}{4}$  as dense and the dose was doubled. The other cultures of which larger doses were injected are Sputum I, Nasua and Cat I (0.75 cc.), and Swine I (1 cc.). More recent tests indicate, however, that any variation in the dose as slight as these has but little influence in modifying the duration of the disease.

As far as practicable, the tests were made as soon as the purity of the cultures was beyond doubt, in order to reduce to a minimum the factor of artificial attenuation. This seems to have been on the whole (p. 471) inconsiderable.† An effort was also made to test the cultures in groups as far as possible, in order to furnish identical conditions. These groups are Bovine I and Nasua, Sputum II and Bovine II, Sputum III and IV, Sputum I and IV, Horse I and Cat I, Sputum V, VI and Bovine III, IV and V. Sputum VII and Bovine VI may be considered a group, though the inoculations were not made simultaneously, owing to

\* *La tuberculose et son bacille*, 377.

† See Table III, Bovine culture I.

an accident. The ages of the different groups of cultures varied from a minimum of 9 to a maximum of 24 days. The total age of the cultures likewise varied at the date of the first test from 1 month and 10 days to 9 months and 25 days. These differences, which were largely counterbalanced by the group inoculations, cannot be dwelt upon here, as the table contains all the information needed for the reader to form his own opinion. It should be stated, however, that the heaviest rabbits of any group were chosen for the bovine cultures. After the inoculation the rabbits were handled very little, in order that the conditions might remain as uniform as possible. For this reason I have no temperature records, but hope to obtain them from a special series of experiments.

The results may be classed as gross or those manifest on ordinary observation and those deducible from a microscopic examination of the diseased tissues and organs. The gross results show a sharp line of demarcation between the bovine and the human cultures. While all the rabbits inoculated with the former succumbed in from 17 to 21 days, of the rabbits inoculated with the latter only one succumbed in 35 days. The others were chloroformed after periods ranging from 1 month and 24 days to 3 months and 18 days. At the time they were killed all but one had increased in weight, some but little, others much.

The rabbits inoculated with bovine bacilli manifested in most cases more or less dyspnoea at the end of 8 or 10 days. The lesions were practically the same in all, with slight minor modifications. The lungs, as the first and chief recipients of the injected bacilli, were in a state of expansions, which in some cases was extreme. All lobes were densely sprinkled over with small grayish tubercles, varying from mere specks to those 1 mm. in diameter. The liver was usually mottled, indicating fatty changes, and in about half the cases it was permeated with barely visible grayish points. The spleen was enlarged to 2 or 3 times its normal size (p. 472) and as a rule permeated with minute tubercles. In the kidneys the visible tubercles were scarce. In 3 cases they were seen in the heart muscle, in several in the follicles composing Peyer's patch at the ileocaecal valve.

The sputum rabbits, with one exception, behaved quite differ-

ently from the bovine cases. A certain number showed signs of illness after 7 or more days. They were quiet, somewhat drowsy and ate little, but manifested no dyspnoea. This condition lasted one or two weeks, after which recovery took place. A certain number did not show this transitory depression. It is probable that with all, during the first month, there was loss of weight, for subsequent weighings showed no gain upon the initial weight. At the time they were chloroformed, they had all more than recovered in weight. The lesions in these rabbits were in many respects quite different from those of the bovine rabbits. The rabbit which received the culture marked Sputum I did not show any recognizable lesions. The difficulty experienced in the attempts to cultivate this bacillus leaves the interpretation of this case somewhat doubtful, although the microscopic preparation from the feeble culture used showed well-stained bacilli. The lesions of the other cases were quite uniform in character.

In all, the lungs contained tuberculous foci sprinkled over the various surfaces from 1 mm. to 1 cm. apart. They did not seem to interfere functionally, for the lungs collapsed normally when the thorax was opened. The tubercles frequently projected somewhat above the surface in the collapsed state of the organ. In the fresh condition the foci were observed as minute dots, barely visible owing to their translucency, as larger foci, 2 mm., in rare cases 3 to 4 mm. in diameter, also translucent excepting the center, which was occupied by a minute opaque point, and as more diffuse infiltrations of a translucent appearance mainly at the sharp lateral margin of the lobes. These different forms of lesions were usually found associated in the same organ, the largest in the animals kept alive longest. Necrosis was an inconspicuous feature, whereas the translucency was often so perfect as to conceal the small lesions from the eye. When placed in alcohol, these became opaque and visible.

The liver usually contained minute tubercles scattered sparsely over the organ. The spleen, only very slightly larger than normal, was affected to nearly the same degree. The kidneys came next to the lungs in the extent of the lesions. Sprinkled sparingly over the cortex were opaque whitish foci from one to

two mm. in diameter. When the organ was incised, these round foci, in many cases, corresponded to radial whitish lines and bands, extending from the periphery towards the pelvis and usually stopping within the medullary portion near its base. More (p. 473) rarely small whitish foci were observed in the walls of the stomach or the large intestine. The lymph nodes were free excepting in one case, in which the node associated with a tuberculous kidney was involved.

In all cases inspection of the affected organs revealed no degenerative changes. They were evidently not disturbed by the focal lesions, an observation strengthened by the increased weight of the animals when sacrificed. The single rabbit which died 35 days after inoculation had received Sputum culture IV. It is worth while to note as a highly probable explanation of this one exception that the rabbit, after inoculation, escaped from the basket in which it was being carried and had to be chased for a long time in the animal room before it could be penned. I at once anticipated some modification of the disease, owing to the different distribution the bacilli would undergo under the influence of muscular exertion. This anticipation was realized. The rabbit after a week became quiet and remained dull and drowsy, without any change in respiration. On the day before death it sat in a crouching position, the hind feet drawn forward under the body, the eyes partly closed. After death its weight was 922 grammes, the initial weight having been 1620 grammes. During the latter weeks a purulent ophthalmia developed in the left eye, and shortly before death there was a slight discharge and beginning opacity of the cornea in the right eye.

In the liver, lungs and kidneys there were minute, translucent tubercles, scarce in the lungs and kidneys, more abundant in the liver. The lesions, found in sections of hardened tissue to be relatively very immature, could not explain the rapid emaciation and death, as they were less extensive than those of the surviving rabbits, unless we assume that the different, more general distribution caused a more rapid breaking up of the bacilli and diffusion of the toxins. Another hypothesis would be the presence of foci in the central nervous system, which was not examined. A

second trial upon a rabbit 2 months later, with conditions as nearly the same as possible, proved no exception to the general rule. The rabbit showed but little disturbance, and was chloroformed after 2 months and 9 days. The lesions found were like those induced by the other sputum bacilli.

In order to probe still farther this difference between bovine and human bacilli, the lungs of all but a few rabbits were subjected to a microscopic study. Here the foci may all be considered primary and produced under like conditions. The lesions as defined in fixed and hardened tissue by the microscope in the bovine cases were characterized by rapid necrosis of the tubercle and the presence of very large numbers of tubercle bacilli. This necrosis was evident in the fresh organs from (p. 474) the marked opacity of the comparatively young tubercles. The tubercle itself at the stage in which it came under observation varied slightly from case to case. It consisted of a necrotic center, absent only in the smallest foci, outside of which a zone of epithelioid cells was distinguishable. This zone was in several cases bounded by a peripheral one of cells having deeply stained nuclei and probably lymphoid. These latter cells were also intermingled with the epithelioid ones. The central necrosis appeared in two forms; it either was characterized by the presence of a very dense, deeply stained mass of nuclear fragments, or else these were present only to a slight degree and the center had a more rarefied aspect. In the latter case it was evident that the necrotic mass consisted of the bodies of epithelioid cells and the few nuclei present. In the former the source of the great mass of nuclear detritus remains in doubt. These dense nuclear masses were present in abundance in Bov. I and III. In Bov. II and IV they were not quite so conspicuous; in Bov. V least so. It is worthy of note here that Bov. I and III are the two cultures which proved rapidly fatal to cattle inoculated with them, as will be shown farther on.

In the series of rabbits inoculated with human bacilli, the lungs present quite different conditions. The lesions evidently develop very slowly, for in the one rabbit which succumbed after 35 days, the tubercles were very small, translucent, the bulk microscopic

in size. With the continued life of the rabbit they grow larger. The microscopic picture differs from that of the bovine series in the rarity of necrosis and in the comparative scarcity of tubercle bacilli. The tubercles consist of aggregations of large epithelioid elements which only in the center of the larger foci show necrosis. These epithelioid foci may be rarely enclosed by a zone of round cells. Giant cells are present, but as a rule in very small numbers. In the Sputum III rabbit they were exceptionally numerous and very large. The contiguous alveoli may be occluded with patches of epithelioid cells not to be confounded with desquamated epithelium.\* Tubercle bacilli are found only in the necrotic centers, either in very small numbers or more abundantly. In some cases they stain feebly. In all cases they are somewhat longer than the bovine bacilli in the same situation.

In addition to the foregoing inoculation tests, made as far as practicable with equal doses, a few others were tried under slightly modified (p. 475) conditions. A large rabbit (No. 20), weighing 2048 grms., received into the abdominal cavity the usual dose, 0.5 cc. of the standard suspension. Death ensued 26 days later. The walls of the abdomen and of the large intestine were densely studded with minute tubercles, the liver permeated with them. The lungs also were densely beset and penetrated with minute translucent tubercles. They did not differ appreciably from the lungs after intravenous inoculation. This mode of inoculation thus proved almost as promptly fatal as the intravenous injection. The same suspension of tubercle bacilli used upon the preceding rabbit was diluted with 9 volumes of bouillon, and 0.5 cc. injected into an ear-vein of a rabbit (No. 27) weighing 1932 grms. The rabbit thus received one-tenth the usual dose. In this animal the symptoms and duration of the disease and the lesions were nearly the same as those of the rabbits inoculated with the horse culture to be described later. The rabbit showed evidences of disease after two weeks, with slowly increasing

\* The lesions in rabbits due to sputum bacilli resemble in many respects those produced by Prudden with boiled and washed tubercle bacilli in the same species, if we exclude the slight progressive tendency of the disease due to the living forms. See N. Y. Med. Journal, 1891, i, 637.



dyspnoea. On the 34th day it was chloroformed, as it would probably have lived but one or two days longer. The extreme relative virulence of the bovine bacilli is thus put into a clear light.

A similar experiment was made with Sputum culture III. One rabbit received an equivalent of the usual dose, another one-tenth of this on March 1st. Both are still alive (July 20), and the initial weights of 1707 and 1672 grms. are now 1558 and 1986 grms.

It has already been stated that the Nasua culture, presumably derived from sputum, produced neither symptoms, nor visible lesions in a rabbit. The swine and the cat culture, however, produced lesions practically identical with those due to the bovine cultures.

The horse culture takes a position midway between bovine and human cultures, so far as the rabbit inoculations shows. These, therefore, deserve a more detailed description. The first rabbit, treated like all the rest, remained apparently unaffected for a month, although the weight had fallen slightly from 1505 to 1477 grms. In the second month respiration became somewhat slower and grew gradually more and more labored, so that the animal had to be chloroformed just two months after inoculation. The weight had fallen to 1232 grms. The lesions were macroscopically unlike those in any other rabbit of the series. In the first place, the lungs failed to collapse even slightly. They are densely beset and permeated with tubercles of a grayish, feebly translucent appearance, the majority about 1.5 to 2 mm. in diameter, coalescing into patches 4 and more mm. in diameter. Minute tubercles are also visible among the larger ones. The latter may have a minute, opaque, necrotic center. The liver is apparently free from tubercles, but the slightly (p. 476) enlarged spleen is beset with sharply outlined, slightly projecting grayish tubercles 1 mm. in diameter. The kidneys are affected in a manner similar to those of the sputum rabbits, but the foci are larger. There are scattering tubercles in the walls of the small and large intestines, but none in the walls of stomach. A second rabbit, inoculated 6 months later, was chloroformed after 40 days

on account of severe dyspnoea. The course of the disease and the lesions were like those of the first rabbit. A noteworthy peculiarity of these cases is the presence of tuberculous foci 2 to 4 mm. in diameter in the superficial axillary and popliteal lymph nodes. These were not seen in any of the sputum rabbits, but were produced by retarding the bovine disease in a rabbit. The intermediate position of this horse culture is well illustrated by this experiment referred to above, in which a dilution of bovine tubercle bacilli, equivalent to one-tenth of the usual density employed, produced manifestly the same effect upon rabbits as the horse culture. In other words, the pathogenic power of the bovine culture as measured upon rabbits was 10 times that of the horse bacilli. Further trials will, perhaps, enable us to give a rough arithmetical ratio between the pathogenic power of the bovine and the sputum cultures as affecting adult rabbits. I do not, however, consider the difference between these races to be solely quantitative.

A comparison of the lesions produced by these three races was attempted by a histological examination of the lungs, spleen, liver and kidneys of three rabbits:

No. 16 Wt. 1527-1617: Sput. V: Chloroformed 3 months 7 days after inoculation.

No. 14 Wt. 1540-1232: Horse I: Chloroformed 2 months 14 days after inoculation.

No. 19 Wt. 1443- Bov. V: Died 20 days after inoculation.

I refrain from giving the detailed account of the lesions in each organ and limit myself to the following summary:

Sputum V. Homogeneous epithelioid cell foci of small size, with very little central necrosis and very few tubercle bacilli. In the lungs and kidneys these foci have lymphoid cell mantles, in the liver well-defined connective tissue capsules.

Horse I. Large foci in lungs, where they are so numerous as to coalesce; some large foci in kidneys; smaller ones in the spleen. In the liver the foci are represented simply by one or several large giant cells, situated within the lobules. Foci large in subcutaneous lymph nodes and Peyer's patch. Necrosis of the

foci quite extensive in all the organs excepting the lungs, where it is slight. Tubercle bacilli fairly abundant in all foci.

(p. 477) Bovine V. Large numbers of epithelioid cell foci in lungs, liver and spleen. In the latter epithelioid cells are also abundant throughout the pulp. Foci small in kidneys. Necrosis under way in lung foci. Tubercle bacilli very abundant in all foci.

Taking into consideration the time during which these lesions developed, we may epitomize the observed differences as follows:

In the first rabbit, very gradual development of the tubercles, with supression of the bacilli and reparative changes leading to a stationary condition of the disease. In the second rabbit, continuous but not very rapid development of tubercles in the various organs. In the kidney and spleen evidences of limitation of the foci. No evidence that bacilli are repressed. In the third rabbit very rapid appearance of the foci, with unchecked multiplication of the bacilli and rapid onset of necrotic changes.

As a matter of some interest there may be briefly mentioned certain lesions of the eye in three of the sputum rabbits. In rabbit No. 7, inoculated with Sputum culture IV, which animal was the only one of all the sputum rabbits to succumb (in 35 days) a purulent ophthalmia appeared in the left eye some time before death. Soon after a slight cloudiness of the cornea of the other eye was noticed. A discharge had started in this shortly before death. I did not associate these lesions directly with tuberculosis, although later cases make it probable that the purulent discharge was secondary to tuberculosis of other parts of the eye. At the autopsy I examined the discharge for tubercle bacilli, but found no acid-resisting bacilli.

The second rabbit (No. 12) inoculated with a culture from the same source first called my attention to this localization of the tubercle bacilli. In this animal there was noticed some weeks after the inoculation, a slight nodular thickening of both lids of the right eye, which slowly grew more conspicuous. Vision became impaired by the enlargement and gumming together of the lids, so that the rabbit used the other eye only. When this animal was chloroformed, 3 flattish, disk-like, firm excrescences

were found on the sclera at the margin of the cornea, about 90° apart. Of these, as well as of the nodulated lower eyelid, sections were made, and both lesions proved to be tuberculous. In both the tubercle bacilli were sparingly present. The neoplasm in the eye-ball had involved nearly the whole thickness of the sclera. In the eyelid the multiple foci were external to the lobules of the Meibomian glands. In still another animal eye lesions were found. About 2½ months after rabbit No. 16 had been inoculated with Sputum culture V, the lids of the left eye were observed to be gummed together. A pasty, yellowish (p. 478) exudate was found under the lids and the cornea was slightly opaque. About 3 weeks later the animal was chloroformed and faint whitish spots were seen in both eyes, presumably on the iris. Sections of the eye hardened unopened in Zenker's fluid confirmed this supposition. Small epithelioid tubercles were found in the vascular stroma of the iris as well as in one ciliary body. Linear infiltration of the cornea was observed, starting from the most affected side and extending to the middle of the cornea. In its course several sections of vessels were found. A similar infiltration had begun from the opposite side. In the foci tubercle bacilli were very scarce. The infection probably came through the blood, as infection from the point of injection on the ear is hardly supposable, since the lesions here are of the slightest character. The animals had been kept separated, and could not have acquired the infection from the exterior. The eye of the rabbit thus seems to be a very vulnerable organ, and earlier experimenters have, in a way, chosen by accident that organ in this species most likely to give positive results.\*

The divergences noticed when rabbits weighing between 1300 and 2200 grammes are inoculated into an ear-vein with 0.5 cc. of a well-clouded suspension of tubercle bacilli in bouillon are as follows:

1. Death of the bovine cases in 17 to 21 days.
2. Rapid evolution and necrosis of the pulmonary tubercles, with very great increase of the tubercle bacilli in them.

\* The eye of Sputum rabbit VII were affected in the same manner.

TABLE III  
*Rabbits*

Culture	Total age of artificial culture	Num- ber of trans- fer	Date of inoculation	Age of culture used, in days	Dose in cc.	Mode of inoculation	Desig- nation of rabbit	Initial weight in grammes	Final weight	Chloroformed after	Died in
Sputum I	10 mos. 27 days.	2nd	June 16, 97.	61	0.75	ear-vein.	17	1470	1681	2 mos. 3 days.	
" II	3 "	5th	Feb. 24, 97.	24	0.5	" "	6	1380	1645	1 " 26 "	
	1 " 19 "	2nd	April 3, 97.	18	0.5	" "	8	1790	1830	2 " 8 "	
" III	13 " 17 "		Mch. 1, 98.	16	1.0†	" "	28	1707		Alive July 20; weighs 1558.	
	13 " 17 "		" "	16	1.0*	" "	26	1672		Alive July 20; weighs 1986.	
" IV	1 " 18 "	2nd	April 3, 97.	18	0.5	" "	7	1620	922		1 mo. 5 days.
" V	4 " 19 "	5th	June 16, 97.	12	0.5	" "	12	1620	1722	2 mos. 9 days.	
" VI	1 " 12 "	3rd	Aug. 26, 97.	10	0.5	" "	16	1517	1617	3 " 7 "	
" VII	1 " 10 "	3rd	Aug. 26, 97.	10	0.5	" "	18	1305	2067	3 " 18 "	
	1 " 19 "	2nd	Mch. 1, 98.	16	1.0†	" "	29	1882	1788	3 " 8 "	
Bovine I	15 " 24 "	14th	Mch. 20, 96.	16	0.5	" "	3	2279	—		17 days.
" II	37 " 27 "	38th	Jan. 25, 98.	12	0.5	" "	24	1795	—		22 "
" III	2 " 7 "	3rd	Feb. 24, 97.	24	0.5	" "	5	1360	—		17 "
	4 " 3 "	5th	Aug. 26, 97.	10	0.5	" "	15	1775	—		21 "
	4 " 23 "	5th	Aug. 26, 97.	10	0.5	" "	17	1607	—		15 "
" IV	9 " 23 "	9th	Feb. 15, 97.	17	0.5	abdomen.	20	2048	—		26 "
	9 " 23 "	"	" "	17	0.5§	ear-vein.	27	1932	1416		Killed on 34th day, very severe dys- pnoea, probably within 24 hours of time of death. 20 days.
" V	4 " 3 "	5th	Aug. 26, 97.	10	0.5	" "	19	1443	—		

Bovine VI	2 mos. 18 days.	3rd	Mch. 15, 98.	13	1. of	ear-vein.	21	2353	1877	1 mos. 24 days.	Chloroformed on 22d day; dying.
<i>Natus</i>	19 " 25 "	18th	Mch. 20, 96.	16	0.75	" "	2	1800	fat condition wt. ?	1 mos. 24 days.	17 days.
Swine I	2 " 6 "	4th	July 14, 96.	12	1.	" "	1	2000(?)	—	"	"
Horse I	{ 5 " 4 "	6th	July 24, 97.	18	0.5	" "	14	1540	1232	2 " 4 "	"
	{ 11 " 5 "	11th	Jan. 25, 98.	12	0.5	" "	25	1653	—	1 " 9 "	"
Cat I	10 " 17 "	5th	Jan. 25, 98.	18	0.75	" "	13	1320	—	"	20 "

\* Dilution about one-twentieth of the standard.

† Dilution about one-fourth of the standard.

‡ Dilution about one-half of the standard.

§ Dilution about one-tenth of the standard.

3. Death of the sputum rabbits (one explainable exception) did not ensue, but after  $1\frac{1}{2}$  to  $3\frac{1}{2}$  months the original weight had been more or less exceeded.
4. The pulmonary tubercles in the sputum rabbit developed very slowly, with very little tendency towards necrosis. The bacilli were present in very small numbers only.
5. The swine and cat cultures are to be classed with the bovine, the horse culture stands intermediate.

(p. 480) *Gray mice*.—White mice have been pronounced quite insusceptible by Koch. Of 5 inoculated subcutaneously with a culture from the monkey, 12 with a culture from miliary tuberculosis, only one of the first set showed a few grayish nodules in the lungs. On the other hand, field-mice were found quite susceptible.

Two parallel tests were made upon gray house-mice with cultures of Bovine V and Sputum VI. At the time control inoculations of the suspensions used were not made upon guinea-pigs, and subsequent developments made it doubtful whether Bovine V was alive. This part of the experiment is therefore omitted from the table given below and a later experiment with Bovine VI substituted. The suspension used in this latter test was employed simultaneously upon 2 guinea-pigs and a rabbit with the usual success.

In the first bovine test the 4 mice inoculated, 2 subcutaneously and 2 into the abdomen, all died, the first on the 8th and the last on the 37th day, without any lesions recognizable with the naked eye. In the cases of the 4 mice inoculated with the sputum culture, death ensued between the 8th and the 40th day. In one of these the lungs contained a number of whitish, rather firm, nodules, 1 to 2 mm. in diameter. In sections these were found to consist of completely necrotic foci, enveloped by a dense, broad zone of pneumonic infiltration, within which all alveoli were filled with nuclear debris. A striking feature were the immense numbers of rather slender, mainly beaded tubercle bacilli, which occupied not only the necrotic center, but in equal abundance the pneumonic periphery. This case proved the vitality of the sputum culture, and the test is therefore inserted in Table IV.

(p. 481) The second bovine test resulted in the death of the two mice receiving the dose into the abdomen, in 5 days. There were no lesions recognizable. The two mice inoculated subcutaneously were active up to the 37th day, when they were chloroformed. Lesions were not found.

*Pigeons.*—Fowls and pigeons have been used with success in distinguishing avian from mammalian tubercle bacilli. Hence it was thought best to test human and bovine bacilli on pigeons.

TABLE IV

*Gray mice*

Designation of culture	Total age of culture	Number of transfer	Age of culture used	Dose and mode of injection	Results
Sputum VI	5 mos. 27 days	6th	24 days	Mouse 1, 0.5 cc. subcut.....	Dies in 34 days, no tuberculosis.
				Mouse 2, 0.5 cc. subcut.....	Dies in 40 days, no tuberculosis.
				Mouse 3, 0.25 cc. abdomen. ....	Dies in 8 days, no tuberculosis.
				Mouse 4, 0.25 cc. abdomen. ....	Dies in 34 days, tubercles in lungs.
Bovine VI	2 mos. 18 days	3rd	13 days	Mouse 5, 0.25 cc. subcut.....	Chloroformed in 37 days
				Mouse 6, 0.25 cc. subcut.....	Chloroformed in 37 days.
				Mouse 7, 0.25 cc. abdomen.....	Dies in 5 days
				Mouse 8, 0.25 cc. abdomen.....	Dies in 5 days

The cultures used are given below in the table. The bacilli, in the form of bouillon suspensions, were injected into the pleuro-peritoneal cavity, the needle being introduced caudad of the sternum. In one case the injection was made into a wing-vein. The inoculations were in general negative, with the possible exception of that of the swine culture. In this bird there was found hyperaemia of the serosa of the intestines, with an eruption of scattering, minute grayish dots. There were similar opaque points on the air-sac membranes. On the duodenal loop were



found some particles of viscid exudate composed exclusively of coarsely granular cells. In this exudate some tubercle bacilli were still recognized by the specific stain. In some of the other pigeons there were a few opacities of the mesenteries and air-sac membranes, with perhaps one or more conspicuous Peyer's

TABLE V

*Pigeons*

Designation of culture	Total age of culture	Number of transfer	Age of culture used	Designation of pigeon	Dose and mode of injection	Remarks
Sput. II	6 mos. 14 days	9th	11 days	No. 2	1 cc. abdomen.	Chloroformed in 45 days: negative.
" III	3 mos. 19 days	5th	11	" 4	1 cc. abdomen.	Chloroformed in 57 days: negative.
Bov. II	5 mos. 26 days	9th	11	" 1	1 cc. abdomen.	Chloroformed in 49 days: negative.
Swine I	1 yr. 19 days	17th	11	" 3	1 cc. abdomen.	Chloroformed in 57 days: minute excrescences on portions of intestine and membranes of air-sacs.
Sput. V.	5 mos.	5th	31	" 5	$\frac{3}{4}$ cc. wing-vein.	Chloroformed in 47 days: negative.
Bov. V.	8 mos. 14 days	8th	24	" 8	1.5 cc. abdomen.	Chloroformed in 49 days: negative.
Horse I	11 mos. 5 days	11th	12	" 7	0.5 cc. "	Chloroformed in 50 days: negative.

patches. Even in refractory animals, lesions such as these might be anticipated where the tubercle bacilli are deposited.

(p. 482) *Cattle*.—It is a noteworthy fact that, in spite of the great economic, agricultural and hygienic interests involved in the diffusion of bovine tuberculosis throughout the world, no experiments upon cattle with cultures of the bovine bacillus had been

made up to the time of my first experiments, published in the *Transactions of the Association of American Physicians* for 1896. Experiments upon cattle with the human bacillus had been made by several observers. A discussion of these tests I shall defer to the end of this article, because of certain secondary questions, which will be clearer when my tests have been described.

The results of the inoculation of two heifers into the lungs with Bovine culture I and *Nasua* culture have already been published.\* It may be stated briefly that the bovine culture produced general tuberculosis, ending fatally in 35 days, while the *Nasua* (human) culture failed to produce any recognizable lesions.

During the warm season of 1897 inoculations were made with 5 sputum, 1 swine and 4 bovine cultures upon as many cattle. For these 10 animals I am indebted to the Massachusetts Board of Cattle Commissioners, who have shown much interest in the progress of these investigations, because of the need felt by them of more definite information upon the relation of bovine tuberculosis to the human disease. The test was carried out in two series, the first including 4, the second 6 animals. The culture material used was suspended in bouillon, as described, the density of the suspension being about the same as that of a typhoid culture in bouillon 24 hours old. In both series the dose was 2 cc. of such a suspension.

Series I. The 4 animals of this series were inoculated with the following cultures:

- Sputum II, total age 5 months 9 days; 8th transfer.
- Sputum III, total age 2 months 15 days; 4th transfer.
- Bovine II, total age 5 months 2 days; 5th transfer.
- Swine I, total age 11 months 23 days; 16th transfer.

The swine culture is probably bovine in origin, and it was used on this supposition. Assuming that tubercle bacilli become slowly weakened (p. 483) in virulence by artificial cultivation, we should endeavor to use cultures as fresh and of as nearly the same age as possible. This theoretical demand cannot be suc-

\* Loc. cit.

cessfully met, because of the many difficulties surrounding such work. Of the 4 cultures used, Sputum II and Bovine II are of nearly the same age, while Sputum III is but half as old as they, and Swine I more than twice as old.

In making the injection, the space between the 6th and the 7th rib was chosen. The needle was inserted about 3 inches above the level of the elbow (olecranon process). It was found subsequently, at the autopsy that the point chosen was too low, and that in all of the animals the needle, leaving the lung intact, pierced the diaphragm. Some of the bacilli were discharged into the muscles of the thoracic wall, some into the abdominal cavity and some into the pleural cavity. Bearing this accident in mind, we may now go to a description of the further history of the inoculated cattle. They were all housed in a spacious, well-ventilated barn in large commodious horse stalls. A piece of ground adjoining the barn was enclosed, and in this the animals spent 6 to 7 hours a day for about 4 weeks. Thereafter the animals were separated into two lots, one lot being out several hours in the morning, the other several hours in the afternoon. The two which received the bovine and the swine culture were allowed to run together, similarly the two which received the sputum cultures. It might be claimed that there was in this arrangement a possible danger of transmitting the bacilli from one animal to another and of infecting the ground. There was no evidence of this at the post-mortem examination, and the arrangement was considered safe at the start because it takes some time for the tuberculous tissue to become disintegrated. It was, however, deemed prudent not to keep the animals longer than 2 months, on account of the imperfect isolation.

In apportioning the cultures to the animals, the sputum cultures were injected into the youngest animals, in order that these cultures might have any advantage likely to accrue from difference in age. Two yearlings (without any permanent incisor teeth) received the two sputum cultures, the bovine culture was injected into a heifer about  $2\frac{1}{2}$  years old, the swine culture into a heifer about 2 years old.

They were killed and examined at the Brighton (Boston)

abattoirs, with the co-operation of the Board of Cattle Commissioners, just two months after the day of the injection. Before injection, these animals had been tested with tuberculin by the Board and found free from tuberculosis. Still, since this agent occasionally allows an animal to escape which contains foci of the disease, attention was directed to this point (p. 484) at the autopsies. No lesion, however, was found which from its situation and appearance could be referred to any former spontaneous infection.

Let us examine first the effect of Sputum culture II and Bovine culture II, which were of nearly the same age when injected.

The weight of the yearling which had received the sputum culture had risen in the two months from 520 to 580 lbs., that of the heifer from 650 to 710 lbs. There was no continuous fever recognized in either animal, though the temperature was taken twice a day, morning and afternoon. The fluctuations noticed were evidently due to the effect of the sun while the animals were in the enclosure.

The lesions in the yearling were very slight. At the seat of inoculation between the 6th and 7th ribs a mass of tubercle attached to pleura about  $1 \times \frac{1}{2}$  inch in dimension, the tubercles composing it partly cheesy, partly firm. Near the cephalic border of ventral lobe of right lung, a subpleural nodule, not yet necrotic, about  $\frac{1}{8}$  inch in diameter. On abdominal aspect of diaphragm, right side, about 24 isolated tubercles  $\frac{1}{12}$ — $\frac{1}{8}$  inch in diameter. A few similar tubercles on the omentum, which is slightly adherent to the large intestine. When adhesion was removed, about 6 or 7 nodules found on caecum  $\frac{1}{12}$  inch in diameter. Evidently the injection needle had passed through the diaphragm into abdomen, depositing some fluid there and some in thorax when partly withdrawn.

The lesions in the heifer which had received the bovine culture were quite extensive and were diffused through thorax and abdomen, owing to the penetration of the diaphragm by the needle of the injection syringe:

*Thorax.*—The right cavity shows an abundant eruption of tubercles along the borders of the ribs. Some of the masses formed are characteristically flattish, grape-like and in bulk quite large. One mass measured  $8\frac{1}{2} \times 3 \times 1\frac{1}{2}$  inches. Others of similar dimensions were present. On the lateral margin of the right lung a series of loosely attached, flattish neo-

plasms up to 2 inches in diameter, besides hyperaemic fringes of loose connective tissue. On the convex surface of this lung only a few tubercles. Large patches of tubercles on pericardium and diaphragm.

In the muscular portion of diaphragm, right side, a mass of tuberculous tissue (probably place where needle penetrated)  $1\frac{1}{2} \times 1\frac{1}{2} \times \frac{1}{2}$  inch in dimension. The caudal of the series of dorsal mediastinal glands about twice normal size on account of the presence of many small foci, showing in some cases an opaque, yellowish centre.

(p. 485) *Abdomen*.—The omentum densely studded with agglomerations of tubercles covering the greater part of its surface. These masses vary up to  $\frac{1}{2}$  inch in thickness. Similar patches on abdominal aspect of diaphragm and on spleen. Fewer patches on gall-bladder and on liver. In one of the portal glands a  $\frac{1}{4}$ -inch focus, pale, grayish, permeated with small calcareous spicules.

The examination of sections of the pleural eruptions and of one of the dorsal mediastinal glands showed the typical lesion of bovine tuberculosis, with its foci of epithelioid cells and its numerous giant cells containing a few tubercle bacilli. Any detailed description of these lesions would be simply a repetition of familiar facts.

We have in these cases a wide divergence in the result of inoculation. The human bacillus produced a slight eruption of small, tubercle-like bodies, which did not present even microscopically the characters of true tubercles, while the bovine bacillus produced an exquisite case of pearly disease both in thorax and abdomen, with the formation of large, grape-like masses in the chest.

The youngest sputum culture (III) was injected into a yearling weighing 410 lbs. At the end of two months the weight had risen to 480 lbs. The lesions found are slight:

On the abdominal aspect of diaphragm, right side, a patch of isolated tubercles about 2 inches in diameter, the tubercles themselves about  $\frac{1}{8}$  inch in diameter and about  $\frac{1}{2}$  inch apart. They are grayish, opaque. At place of inoculation, on serous aspect of ribs, a flattish neoplasm 1 inch in diameter and about  $\frac{1}{8}$  inch thick. Other lesions not detected. In this case also the needle evidently entered abdomen through diaphragm. Sections made

from the small isolated tubercles on the abdominal surface of the diaphragm show them to be masses of newly forming tissue. They consist in the main of spindle-shaped connective-tissue cells running in parallel and interlacing groups and richly supplied with vessels. No trace of the characteristic tubercle formation or of bacilli, although these bodies are evidently due to the bacilli injected.

The swine culture was injected into a somewhat older animal weighing 620 lbs. After two months the weight was 660 lbs. The autopsy showed the following conditions:

At place of inoculation (right chest wall) a subcutaneous tumor about 2 inches in diameter, made up of a very dense connective-tissue sac,  $\frac{1}{4}$  inch thick, which encloses a pale yellowish semifluid mass (caseous). There are besides this focus, in the same situation, 3 smaller nodules from  $\frac{1}{2}$  to  $\frac{3}{4}$  inch in diameter, the largest with caseous centre. On the pleural aspect a similar  $\frac{1}{2}$ -inch centrally softened focus.

(p. 486) In nearly the centre of the right half of diaphragm and projecting into abdomen for  $\frac{1}{2}$  inch is a tumor representing portion of a larger focus in the muscular portion of the diaphragm about 1 inch in diameter. This focus is likewise caseous, diffuent centrally. On all the ribs of right pleural cavity are eruptions of small tubercles, reaching in some instances a diameter of  $\frac{1}{8}$  inch. Besides the palpable tubercles, there is along one border of each rib a line of vascular fringes of connective tissue. In many of these fringes tubercles are not noticed, although the fringes themselves are evidently a result of the injection.

Along the lateral border of the right lung similar vascular fringes of tissue containing tubercles. These fringes extend dorsad for about 2 inches on ventral and cephalic lobes.

Diffuse eruption of minute tubercles on pleural aspect of diaphragm, right half.

Large caudal mediastinal gland contains large numbers of tubercles, varying in size from mere points to those  $\frac{1}{8}$  inch in diameter and showing beginning necrosis. Left bronchial gland several times normal size. Ventral mediastinal gland several times normal size and containing several large, centrally caseous foci. One mesenteric gland contains several small necrotic tubercles.

In this case many of the bacilli had been deposited in the fleshy portion of the diaphragm and some under the skin, and had thus

been prevented from exerting their greatest power. Sections were made of the subcutaneous foci, the anterior mediastinal and bronchial lymph-glands and of the vascular fringes on the pleural aspect of the diaphragm. The glandular and subcutaneous lesions are characteristically tuberculous, with a greater tendency towards necrosis and disintegration of the tubercles than in the animal inoculated with Bovine culture II. The lesions of the serous membranes are more vascular and show greater tendency toward the formation of connective tissue around the minute tubercles. In general this culture must be considered less potent than the bovine culture. Whether this is due to the more prolonged artificial cultivation or to the species through which the bacillus had passed remains unsettled.

Series II. In this experiment three sputum and three bovine cultures, recently isolated, were used. The bovine cultures were of nearly the same total age. The sputum cultures differed somewhat from them and from one another in this respect.

Sputum IV, total age 6 months 10 days, 7th transfer.

Sputum V, total age 1 month 19 days, 3rd transfer.

Sputum VI, total age 1 month 12 days, 3rd transfer.

Bovine III, total age 4 months 7 days, 5th transfer.

Bovine IV, total age 4 months 3 days, 5th transfer.

Bovine V, total age 4 months 3 days, 5th transfer.

(p. 487) The cultures used for the injection were all 9 days old, grown on the same lot of dog's serum. Control inoculations of guinea-pigs and rabbits will be found on tables II and III. The animals at my disposal, unfortunately, varied considerably in age, and in assigning the cultures the advantage was given to the human cultures:

Sputum IV, yearling, 525 lbs. no permanent incisor teeth.

Bovine III, yearling, bull, 645 lbs., no permanent incisor teeth.

Sputum V, cow, 675 lbs., about 4 years old.

Bovine IV, cow, 850 lbs., about 12 years old.

Sputum VI, cow, 865 lbs., about  $3\frac{1}{2}$  years old.

Bovine V, cow, 875 lbs., about 6 years old.

The injection of the cultures was carried out as in Series I, excepting that the point of insertion of the needle was chosen higher up, about 11 inches above the elbow of the animal when in the standing position, between the 7th and 8th ribs. The length of the needles used was about 2 inches. The care of the animals was the same as that bestowed on the preceding lot, excepting that the bovine and the sputum animals were kept separate in the out-door enclosure from the start, the one lot being out in the morning, the other in the afternoon. They were kept two months, with the exception of the young bull, which died 17 days after the inoculation. The four cows of this lot gave at the start altogether about 8 quarts of milk. The secretion was slowly dried up, so that in the sixth week a very little, amounting perhaps to one quart in two days, was removed. The milking was continued chiefly to prevent any udder trouble during the experiment and to maintain normal conditions. The temperature was taken but once a day, at noon.

In comparing the temperature records of these 6 animals it was noticed that the three animals which received the bovine cultures had a high temperature immediately after the inoculation, which lasted until the death of the bull and about three weeks for the remaining two animals. At the same time no such elevation of temperature was recorded for the animals receiving the three sputum cultures. There was but one well-defined rise of temperature in the case of the yearling, from the 13th to the 16th day after inoculation. The other irregularities are probably due to the fact that the temperature was usually taken after these animals had been in the enclosure in the sunshine for several hours. Those with the high temperature were kept much of the time in the cool barn in the morning, which probably depressed the fever curve somewhat. After the period of fever, no other elevations were noted up to the close of the experiment.

(p. 488) The young bull, inoculated with Bovine culture III, showed besides the prompt onset of a high temperature, general and local disturbances about a week after the inoculation. The breathing became rapid, the appetite had partly gone. Emacia-



tion and weakness supervened. He was unable to get up September 11, and died the following night.

The autopsy revealed a severe miliary tuberculosis of both lungs with marked congestion and oedema of the organ. Normal collapse no longer possible. The associated lymph-glands were much enlarged and infiltrated with minute tubercles. Patches of minute tubercles were found on the pleural covering of ribs and on the omentum. Sections from the lungs, dorsal mediastinal glands, pleural neoplasms, liver, spleen and kidneys were examined. In the lungs, mediastinal glands and pleural neoplasms, tubercles are very numerous, in the liver less abundant. In the kidney sections none were seen. In these different situations the tubercles presented nearly the same peculiar features, which distinguished them readily from the tubercles of the spontaneous disease in cattle. To make the differences clearer, a brief description of the lesions in a spontaneously diseased lymph-gland may not be out of place.

A rarefied area within the follicle containing a few nuclei having the characters of endothelioid nuclei and belonging to what are generally known as epithelioid cells, which are imbedded in or whose outlines are fused with a matrix appearing either homogeneous or else very delicately reticulated. In larger foci this rarefied area contains also one or more giant cells whose body is frequently seen merging by prolongations into the reticulated matrix of the tubercle. Among the epithelioid nuclei are isolated nuclei closely resembling those of lymphoid cells. The largest foci are centrally necrotic, that is, they contain a coarse trabecular matrix staining with eosin and picric acid and containing scarcely any nuclei and very little, if any, fragments of nuclear origin. In this mass tubercle bacilli are rarely found. In the lesions of the bull the tubercles have in the first place no giant cells. The new tissue appears to be made up of cells resembling the usual epithelioid cells of tubercle, but much more crowded together and with less definition of the cell outlines. The nuclei are mostly distorted, drawn out, band-like or horse-shoe-like, and twisted into various bizarre forms. Condensation and fragmentation of the nucleus are also seen. In the tubercles in all situations much

fibrin is demonstrated by Weigert's stain. This is especially distinct in the liver tubercles. Here the intercellular substance from material hardened in alcohol stains deeply in eosin. In sections subjected to Weigert's (p. 489) fibrin stain, this substance is blue, appearing throughout the tubercle both as a delicate mesh and as very coarse trabeculae. In material hardened in Zenker's fluid the fibrin stain is less pronounced. In all the tubercles, large numbers of tubercle bacilli are present. These differences are probably due to the rapidity of the process.

On October 27, the remaining five animals were killed at the Brighton abattoirs, with the co-operation and assistance of the Board. The three sputum animals had all gained in weight:

Yearling (Sputum IV) from 525 to 610 lbs.

Cow (Sputum V) from 675 to 750 lbs.

Cow (Sputum VI) from 865 to 960 lbs.

Sputum culture IV. One permanent incisor on the right has appeared since date of inoculation. In utero a foetus about three months old. At point of inoculation in the subcutaneous tissue a small nodule about  $\frac{1}{4}$  inch in diameter with contents soft, cheesy. Attached to this another, smaller nodule about  $\frac{1}{8}$  inch in diameter.

On the right side of chest wall, pleural aspect, there are attached along the six caudal ribs, soft dark red, pendulous masses of newly-formed, highly vascular connective tissue. At point of inoculation, between 7th and 8th ribs, a flattish pediculated mass of tissue of brownish red color. On the 10th rib another mass about  $\frac{3}{8}$  inch in diameter. The left side of thorax is normal.

Right lung. On the smaller (cephalic and ventral) lobes, newly formed delicate fringes of hyperaemic connective tissue, which appears also along the free lateral margin as a delicate band about  $\frac{1}{2}$  inch broad, as well as on a portion of the convex surface of the lung, occupying exclusively the lines representing the boundaries of the lobules.

In the large caudal lobe, which is similarly beset with the vascular fringes, a tumor, representing the place where needle penetrated the lung tissue, projecting slightly above the convex surface, is found two inches from the caudal tip. This tumor, about  $\frac{3}{4}$  inch in diameter, contained a completely disintegrated mass and about a dozen surrounding foci,  $\frac{1}{16}$  to  $\frac{1}{8}$  inch in diameter, with yellow softened centres. On the margin of this same lobe, in addition to the vascular fringes, are four

firm masses of grayish tissue, smooth, flattish, attached by pedicles to the margin of the lobe. The diameters of the largest are  $\frac{1}{4}$  and  $\frac{1}{2}$  inch.

On large (caudal) lobe of left lung there is only a very little development of vascular fringes. Imbedded in the same lobe near lateral margin is a uniformly grayish, slightly translucent mass, sharply defined from the enveloping normal lung tissue. Sections of this focus showed a peculiar lymphoid structure of the tumor, in the centre of which a parasite was lodged. Not (p. 490) having any relation to the inoculation disease, it need not be further discussed.

Attached to the cephalic lobe of the left lung by a pedicle is a small, flattish, smooth mass of new tissue.

The pleural aspect of diaphragm and portions of the pericardium are covered with areas of the highly vascular neoplastic tissue. In some, small nodules can be felt at the free extremity of this tissue.

On the right ventricular surface of the heart four flattish, pediculated masses about as large as split peas are attached.

The various lymph-gland systems, ventral and dorsal mediastinal and bronchial glands, do not show the presence of tubercles or any augmentation in size.

Of this case, sections of the primary lung focus, of two of the pediculated bodies (one from the lung, one from the rib) and of the vascular fringes from the lateral border of the lungs were examined.

The small foci immediately bordering the disintegrated primary focus vary from 0.2 to 2 mm. in diameter. The smallest do not differ essentially from ordinary tubercles, excepting in the scarcity of giant cells. The larger ones are centrally necrotic, with a marked tendency towards encapsulation on the periphery by the condensation of circularly disposed, fusiform, connective-tissue cells. In the smallest tubercles, bacilli are scarce, in the largest they are numerous within the necrotic centre, where they appear as slender, often bent, sometimes fragmented and rather feebly stained rods. In the surrounding epithelioid zone a few well-stained bacilli are present. Passing from the primary place of deposit, the only other lesions are those of the pleura. These occur in two forms, as vascular fringes and as firm, smooth, pediculated bodies, some flattish, like pumpkin seeds in size and outline.

The vascular fringes occur: 1. As mere endothelial tubes; 2. As such enveloped by a layer of wavy fibrillar tissue and covered with a layer of endothelial cells; and 3. As vessels sheathed with a zone of round cells, proliferating endothelial and connective-tissue cells in addition to the fibrillar tissue. Acidophile, polymorphous leucocytes

are present here and there throughout the granulation tissue. Mitoses are occasionally seen. After a prolonged search through 7 sections, one minute rarefied area is detected. In it evidently a tubercle bacillus with long axis nearly at right angles to the section.

The vascular fringes from the thoracic aspect of the diaphragm are like those from the lungs. In the former no signs of tubercle formation.

Sections from one of the neoplasms attached to the ribs show two fairly distinct regions, an outer of dense connective tissue and an inner made up of foci of lymphoid elements and a central necrotic core. This latter body was evidently a vascular offshoot of the pleura, which, before necrosis, had attached to or imbedded in it many lymphoid cells, for the necrotic core contains much nuclear matter traceable to such cells. This core is partly enveloped (p. 491) by a ring of epithelioid cells with nucleus at the outer free end, like those around a foreign body. Some are multinuclear and resemble giant cells. In the zone immediately outside of this cellular ring are several characteristic giant cells. There are no tubercle bacilli, nor is there any tissue recognizable as epithelioid and identifiable as tubercle.

Development of vascular fringes along one border of ribs of the right side of thorax as in preceding case, but amount relatively slight. In the intercostal muscles at the point of inoculation a mass of perhaps a dozen small grayish tubercles.

Sputum culture V. Cow about 4 years old. In utero a foetus 3 to 4 months old.

In the large caudal lobe of the right lung, in the same situation as in preceding case, a projecting tumor about 1 inch in diameter. When incised it is found composed of two  $\frac{1}{2}$ -inch foci of disintegrated, cheesy-viscid matter enclosed in thin, smooth capsules. No surrounding infiltration. Along the margin and on the caudal surface of this lobe, slight development of pendulous vascular tissue and a sessile tubercle about 4 mm. in diameter. On the left caudal lobe only very slight production of vascular tissue.

On the surface of one of the middle dorsal mediastinal glands an aggregation of minute tubercles, the whole about  $\frac{1}{2}$  inch in diameter. Imbedded in the cortex of the same gland two minute tubercles.

In this animal the disease of the middle mediastinal gland, although very slight, is shown in sections to be tuberculosis. The lesions are not to be distinguished from those of the spontaneous disease in cattle,

excepting in the presence of considerable numbers of tubercle bacilli. The tubercles themselves contain the usual number of giant cells, and the largest ones are centrally necrotic, the necrosed mass being indistinctly fibrillar in character, staining deeply with eosin and devoid of nuclear debris. The bacilli in this mass stain rather feebly when compared with the deep stain of those in the giant cells on the periphery of the tubercle. This lesion will be again referred to in summing up the experiments.

Cow (Sputum culture VI). In utero a foetus about four months old.

Within the thorax on the right side, between the 7th and 8th ribs, is a small pediculated, blackish (haemorrhagic) mass of firm tissue about as large as a pumpkin seed, another on the 10th rib. On most of the ribs behind the 7th are gelatinous-looking pendulous vascular fringes of neoplastic tissue. On the pleural surface of the diaphragm a similar development of vascular tissue and several firm, pediculated masses like those on ribs.

On the right lung the cephalic lobe shows very slight formation of marginal fringes. In the ventral lobe whose tip is adherent to the pericardial fat, a uniformly grayish, sharply defined focus  $\frac{1}{4}$  inch in diameter.

(p. 492) In the same situation as in the preceding cases the caudal lobe shows a slightly projecting tumor about  $1\frac{3}{4}$  inches in diameter externally. When incised it is found to consist of a smooth-walled sac  $1\frac{1}{4}$  inches in diameter, containing a yellowish curdy mass, together with a little turbid fluid. No surrounding infiltration. On the convex surface of this lobe there is a slight growth of vascular tissue. Near the caudal tip a flattish mass, partly yellowish, partly blackish, attached by loose tissue to the margin of the lobe. It is about 1 inch long and  $\frac{1}{2}$  inch thick.

In the abdomen, a flattish, sessile mass of pinkish-gray tissue about  $\frac{3}{4}$  inch in its longest diameter, attached to omentum.

In this animal, sections of the grayish focus in the ventral lobe of the right lung and of the suspicious sessile mass on the omentum demonstrate the fact that both lesions are parasitic in origin and due to the same cause as the lung focus in cow inoculated with Sputum IV. Both foci are made up of spherical agglomerations of lymphoid cells, in the centre of which the parasite is situated.

The largest of the pendulous masses from the lungs was examined microscopically and found to be similar in structure to those already described. It consists chiefly of a connective-tissue stroma of interlacing fibres in which are imbedded many capillaries. Scattered through the inner half of the mass are quite small foci of epithelioid and lymphoid cells, but giant cells are absent. In these foci, a few tubercle bacilli are found. The periphery of this pendulous mass consists of circularly condensed connective tissue, beneath which is a homogeneous, somewhat reticulated substance, staining well with eosin and enclosing a few tubercle bacilli. It is probably a layer of fibrin undergoing hyaline degeneration. Small areas of it are still stainable with Weigert's fibrin stain.

Of the three animals receiving bovine tubercle cultures, the fate of one (young bull No. 71) has already been given. The two other cases remained stationary in weight:

No. 88—original weight 850 lbs.; weight at end of experiment 850 lbs.

No. 63—original weight 875 lbs.; weight at end of experiment 870 lbs.

The autopsy notes are in brief as follows:

No. 63 (Bovine culture V). White cow, spotted with red. Horns sawed off. Probably six years old. Foetus in utero about two months old.

*Thorax*.—Right lung adherent to chest wall in several places. At point of inoculation, between 7th and 8th ribs, an excrescence of the costal pleura about  $\frac{3}{4}$  inch in diameter, of dense, pearly-looking connective tissue enclosing a disintegrated mass. Numerous masses and aggregations of small tubercles on all ribs. These masses in some cases are several inches in length. The left side of thoracic wall, below the level of the point of inoculation on (p. 493) the opposite side, is covered with a uniform, pinkish-gray deposit of very minute tubercles. Eruptions of tubercles on pleural surface of diaphragm and on pleural covering of dorsal mediastinal space.

On caudal lobe of right lung a considerable number of tubercular masses, flattish, sessile, from  $\frac{1}{8}$  to  $\frac{3}{4}$  inch in diameter. Between the cephalo-lateral border of this lobe and the pericardium is a mass of newly formed tissue, dense, in which are imbedded many minute yellow tubercles and masses of pericardial fat. The whole is about as large as a fist. It binds the lung tissue, pericardium and diaphragm together. Many tubercles on the caudal surface of this same lobe. There

is no distinct focus in this lobe as a result of the injection, and it is probable that much of the fluid was deposited in the pleural cavity. But palpation reveals throughout both lungs small shotlike bodies in close proximity. On section numerous yellow tubercles from  $\frac{1}{32}$  to  $\frac{1}{16}$  inch in diameter are found imbedded in the lung tissue of all lobes.

The dorsal mediastinal lymph-glands are all several times their normal dimensions. They contain many coalescing yellow tubercles. The ventral (anterior) mediastinal glands are similarly enlarged and the cut surface shows a uniformly cheesy parenchyma.

Minute grayish points under the capsule of the liver.

In the spleen, all Malpighian bodies converted into tubercles with yellow opaque centre. In left kidney several minute grayish tubercles.

Of this case, sections of the left lung, left costal pleura, the large caudal mediastinal gland and the spleen were examined.

The tubercles from the lungs do not differ from those found in spontaneous tuberculosis. The centre is as a rule necrotic and contains a few tubercle bacilli. Outside of this is a zone of nuclear fragments and entire nuclei, shading off into a peripheral zone of epithelioid and lymphoid cells and cells with spindle-shaped nuclei. Giant cells are present in nearly all the tubercles. The new growth on the left side of the thorax consists essentially of newly formed vascular fringes, in which are imbedded minute tubercles with scarce bacilli and occasional giant cells.

In the caudal mediastinal gland the tubercles vary from a mere giant cell to those 2 mm. in diameter and centrally necrosed. The latter are like those in the lung tissue. The bacilli in some necrotic foci are numerous, in others few in number.

In the spleen the follicles contain epithelioid cell foci, some of which are centrally necrosed and which contain many bacilli.

No. 88 (Bovine culture IV). Red and white cow. Teeth very much worn, probably 12 years old, dehorned. Not pregnant.

No deposit in subcutis at point of inoculation. The eruptions of tubercles on the costal pleura of the right and the left side are in character very much like those of the preceding case (No. 63), but less extensive.

(p. 494) *Right lung.* Lobes adherent to pericardium. Adhesions readily severed. On convex surface of the caudal lobe of this side a considerable number of flattish sessile tubercles from  $\frac{1}{16}$  to  $\frac{1}{2}$  inch broad. The caudal aspect of this lobe is similarly beset with them, but in less abundance. Along the margin of this lobe are loosely attached, small, elongated masses of tubercles.

At the same situation in this lobe as in the sputum cases, there is a fluctuating tumor, about two inches in diameter, slightly projecting. It consists of a capsule with nearly smooth walls enclosing a soft caseous mass. It is surrounded by a zone of small necrotic tubercles and with lobules containing numerous minute, grayish foci.

On the cephalic lobe of the right lung are a considerable number of grayish tubercles. Throughout all lobes are scattering tubercles in the lung tissue, some very minute, others larger and opaque, yellowish in color.

The pleura in the dorsal mediastinal space is beset with a large number of small tubercles; similarly the pericardium. The right half of the diaphragm is beset with flattened aggregations of tubercles. Between the ventral lobe of the right lung and the pericardium, and fastening them together, is a mass of newly formed connective tissue and fat enclosing numerous softened foci.

The large dorsal mediastinal lymph gland is enlarged and contains a large number of yellow tubercles. The central portion of the gland is uniformly caseous. In the left bronchial gland a small number of tubercles; in the ventral mediastinal glands a considerable number. Organs of the abdomen appear free from tuberculous changes. Of this case only the tubercles disseminated through the lungs were examined microscopically. For this purpose the left lung was chosen. The tubercles are small, compact up to 1 mm. in diameter. In structure they are indistinguishable from the spontaneous bovine tubercles. The bacilli in them are few in number, rather short, thick and deeply stained.

A summary of the outcome of this last experiment may now be made. The points of difference between the inoculation disease produced by bovine and by human (sputum) bacilli are several.

1. The bovine cases either remained stationary in weight or lost slightly, while the sputum cases gained 75 to 85 pounds. Still, the age of one of the bovine cases may be partly responsible for stationary weight.

2. There was a marked fever in the bovine cases for three weeks after the inoculation; practically none in the sputum cases.

3. There were well-marked differences in the lesions produced. In the sputum cases the lesions are nearly the same and consist in:



(p. 495) (a) A tumor in the right caudal lobe of the lung, about 1 inch in diameter, projecting somewhat above the surface of the lung. This represents the place where the needle penetrated into the lung tissue and deposited the tubercle bacilli. In each case the contents of this tumor were softened and converted into a curdy mass, enclosed in a thin-walled capsule, smooth internally. The disease was not spreading from this point nor were tubercles visible in the lymph glands of the lungs and thorax, excepting in one gland of No. 39 (Sputum V).

(b) The free margin of the right lung and the pleural covering of the ribs on the right side were beset with a new formation of loose vascular fringes or shreds in which in only one case some minute nodules could be felt, and some flattish, pediculated masses, which did not resemble tubercles at all histologically, or which were only abortive forms of the same.

Among the bovine cases we have the following characteristic points to note:

(a) Disseminated tuberculosis of the lungs, severest and fatal in No. 71, the youngest; least pronounced in the oldest, No. 88. Associated with this a local disintegrated focus in the lungs of No. 88.

(b) Tubercular deposits on lungs, pericardium, diaphragm and the ribs, resembling closely the product of the natural disease in cattle. Extension of the eruption to the costal pleura of the left side.

(c) Extensive tuberculosis of all or nearly all the lymph glands of the thorax, including both mediastinal chains.

(d) Slight tuberculosis of other organs, spleen, liver, kidney, in two out of three cases.

A summary of the three separate tests on cattle (including the published experiment), in which twelve animals were used, shows that 6 animals were inoculated with human bacilli, 5 with bovine bacilli; 1 animal was inoculated with swine bacilli.

Of the sputum cases, 1 showed no disease; 2 showed very slight lesions; 3 showed only local lesions without dissemination.

Of the bovine cases, 2 died of generalized disease; 2 showed extensive lesions; 1 showed less extensive lesions.

Designation of culture	Total area of culture		Number of transfer	Age of culture used	Amt. of suspension of bacilli infected	Designation of animal	Age, etc.	Original weight in pounds	Final weight in pounds	Date of inoculation	Result
	mos.	days		days							
Bovine I	5	4	3rd	10	4 cc.	No. 284	heifer, 2½ yrs. old, common stock, pregnant.	(?)	(?)	May 4, 1895	Died in thirty-five days of generalized tuberculosis.
<i>Nasuta narica</i>	9	9	8th	10	4 cc.	No. 300	heifer, 2½ yrs. old.	(?)	(?)	May 4, 1895	Killed June 27, 1895, no lesions.
Sputum II	5	9	8th	9	2 cc.	No. 2616	yearling.	520	580	May 1, 1897	Killed July 1, 1897, lesions very slight.
Sputum III	2	15	4th	9	2 cc.	No. 2634	yearling.	410	480	May 1, 1897	Killed July 1, 1897, lesions very slight.
Bovine II	5	2	5th	9	2 cc.	No. 2635	heifer, 2½ yrs. old.	650	710	May 1, 1897	Killed July 1, 1897, extensive pearly disease in thorax and abdomen.
Swine I	11	23	16th	13	2 cc.	No. 2672	heifer, 2 years old.	620	660	May 1, 1897	Killed July 1, 1897, well-marked pleural tuberculosis with invasion of lymph glands.
Sputum IV	6	10	7th	9	2 cc.	No. 79	yearling, about 1½ years old.	525	610	Aug. 26, 1897	Killed Oct. 27, 1897, abscess in lungs at point of injection, new vascular tissue on ribs and lungs.
Sputum V	1	19	3rd	9	2 cc.	No. 39	cow, 4 years old.	675	750	Aug. 26, 1897	Killed Oct. 27, 1897, lesions same as preceding.
Sputum VI	1	12	3rd	9	2 cc.	No. 76	cow, 3 years old.	865	950	Aug. 26, 1897	Killed Oct. 27, 1897, lesions same as preceding.
Bovine III	4	7	5th	9	2 cc.	No. 71	bull, yearling.	645	575*	Aug. 26, 1897	Died Sept. 12, 1897, disseminated tuberculosis of lungs, liver.
Bovine IV	4	3	5th	9	2 cc.	No. 88	cow, about 12 years old.	850	850	Aug. 26, 1897	Killed Oct. 27, 1897, many minute tubercles in lungs, tuberculous deposits on pleura.
Bovine V	4	3	5th	9	2 cc.	No. 63	cow, about 6 years old.	875	870	Aug. 26, 1897	Killed Oct. 27, 1897, disseminated tuberculosis of lungs and spleen.

\* Two days before death.

In the swine case the lesions were less extensive than in the bovine cases.

(p. 497)

#### ON THE SIGNIFICANCE OF VARIETIES AMONG TUBERCLE BACILLI

The foregoing experiments, while they show unmistakably the close relationship existing among the various cultures studied, nevertheless justify us, if only to guide and stimulate further study, in establishing a distinctively human or sputum and a bovine variety of the tubercle bacillus. It might be better to omit the host designation of such varieties, in order to anticipate assumptions that they are necessarily limited to the host whose name they bear. Still, the convenience of using the host's name is so great that I shall succumb to it. The characters upon which the bovine variety may be based reside, morphologically, in the invariably short, straight form and in the greater resistance of this form to modifying influences of culture-media; biologically, in a greater resistance to artificial cultivation and in a much greater pathogenic activity towards rabbits, guinea-pigs and cattle.

There is proof, furthermore, of the existence of slightly varying characters even within the varieties proposed. Among the bovine forms studies, slight variations in virulence were noticeable. Among the sputum forms, variations in size, in capacity for cultivation, and in pathogenic activity have been observed. The differences between Sputum culture I, on the one hand, and Sputum cultures II to VII, on the other, are quite pronounced. In spite of these variations, mammalian tubercle bacilli may still be considered as forming a fairly compact group when compared with the tubercle bacilli of birds, which are but slightly virulent towards the guinea-pigs, so susceptible to the mammalian type.\*

In regard to the bovine and the sputum varieties, I have, in a former paper, pointed out certain differences of behavior in the

\* I have, unfortunately, been unable to study avian bacilli in connection with the series of this article, because opportunities for making cultures from fowls were wanting. The study of cultures of unknown or indefinite history I have not regarded as likely to yield trustworthy evidence.

body which may be of considerable significance in explaining *their divergent characters*. In an *organism* like the human body, manifesting a certain amount of resistance to the tubercle bacillus, the sputum type multiplies only to a limited extent, unless it can produce dead tissue or gain an (p. 498) exit upon mucous membranes secreting pathological products, where it seems to flourish as a saprophyte. Similar conditions are now and then observed in animals inoculated with human bacilli. Immense numbers of bacilli are occasionally found in necrotic foci, but very few in the surrounding zone of living tissue. In the many sections examined recently, the necrotic foci were the ones in which human bacilli were to be found, if detected at all. The bovine type differs from the former in a far less saprophytic growth. In the pathological secretions and in the caseous masses the bacilli are relatively scarce. This difference may be a result of their adaptation to the bovine body, in which cavities of the lungs and catarrh of the air tubes are far less common. In other words, certain differences in the type of reaction tend in the one case to make the human bacillus more saprophytic, the bovine more parasitic.

Coming to the more practical aspect of this subject, we may present, in view of the relationship between the bovine and the sputum variety of the tubercle bacillus, two propositions for discussion:

1. The sputum bacillus is incapable of finding a foothold in the bovine body.
2. The bovine bacillus may pass to the human subject, owing to its higher pathogenic power.

The transmission of human tuberculosis to cattle has been experimentally assayed by Bollinger, Crookshank, Baumgarten, Sidney Martin, the writer and Frothingham.

Bollinger\* reported in 1894 an experiment performed in 1879. A calf three months old was inoculated into the peritoneal cavity with fluid from a tuberculous human lung. The calf was killed in 7 months. On the mesentery and the peritoneal covering of the

\* Münchener med. Wochenschr., 1894, No. 5.

spleen there were found pediculated tumors from the size of a pea to that of a walnut. The microscopic appearance corresponded completely with that of the spontaneous pearly disease of cattle. The retroperitoneal and mesenteric glands were tuberculous. All others were normal. The little drawing which Bollinger published with the article gives one the impression of smooth, roundish tumors similar to those I have described as resulting from the injection of Sputum cultures IV and VI. They have not the (p. 499) nodulated appearance presented by the spontaneous eruptions or those produced by bovine cultures.

Crookshank\* injected sputum containing numerous tubercle bacilli into the peritoneal cavity of a calf. The calf died after a prolonged illness on the 42nd day.

Extensive lesions were discovered at the post-mortem examination. The mesentery was adherent to the rumen; the liver was adherent to the diaphragm. There was extensive tubercular deposit at the seat of inoculation and an abscess the size of a walnut. Extending over the mesentery from this point there were hundreds of wartlike, fleshy new growths, some quite irregular in form, others spherical or button-shaped. There were similar deposits on the under surface of the liver, on the spleen, in the gastro-splenic omentum and on the peritoneal surface of the diaphragm. The spleen was adherent to the rumen, and on dissecting away the adhesions, another abscess was opened. On the under surface of the liver was a third abscess about the size of one's fist, which burrowed in the depth of the liver substance.

On microscopic examination, extremely minute tubercles were found disseminated throughout the lungs and liver. Tubercle bacilli were found in these organs and in the peritoneal deposits. The pus from the liver abscess contained streptococci. The calf died of pyemia, a result to be anticipated if sputum be employed for inoculation, but sufficient time had elapsed for pronounced local infection leading to acute miliary tuberculosis.

I quote this experiment more fully so that it may discredit itself as a means of deciding whether sputum can produce general miliary tuberculosis in cattle. We know as yet too little of the influence of concurrent infections to place any reliance upon the

\* Trans. Pathol. Soc., London, 1891, 332.

outcome of this experiment as a demonstration of the transmissibility of human bacilli to cattle.

Baumgarten\* briefly mentions an experiment in which human bacilli to cattle in cultures had but little local effect after intra-ocular inoculation upon a calf. Material from a bovine pearly nodule produced typical local and general miliary tuberculosis in another calf.

Sidney Martin† fed one kilogram of tuberculous material from a cow to 4 calves at one meal with their food. Within 4 weeks tubercles were found in the Peyer's patches, mesenteric and bronchial glands and in the lungs of one animal. After 8 weeks, another calf presented the same lesions plus tuberculosis of the posterior mediastinal and the cervical (p. 500) glands. The third calf, killed after 12 weeks, showed ulceration of the small intestine and caecum and lesions of the pleura, besides those mentioned above. The fourth calf, killed after 37 weeks, had tuberculosis of the pleura in addition to that of the various lymph glands already mentioned.

Four calves were fed at one meal with 70 cc. of sputum containing a large number of tubercle bacilli. Three calves, killed after 4, 8 and 12 weeks respectively, had 53, 63 and 13 nodules respectively in the small intestines, chiefly in Peyer's patches. In the fourth calf, killed after 33 weeks, no lesions were found.

Two calves received at one feeding 440 cc. of sputum, containing a large number of tubercle bacilli. In one calf, killed in 8 weeks, 13 tuberculous nodules were found in the intestine. The mesenteric glands were also affected. The other calf, killed in 19 weeks, was found without any lesions.

The author infers from these experiments that "in the case of tuberculous sputum we are dealing with material which is less infective to calves than bovine tuberculous material."

Frothingham‡ carried out some experiments of a similar character for the Mass. Cattle Commission. A culture of human

\* Jahresbericht for 1891, footnote, 666.

† Report of the Royal Commission on Tuberculosis, 1895. Appendix p. 15.

‡ Report of Mass. Cattle Commission for 1897. See also *Zeitschr. f. Tiermed.* 1, 1897,

bacilli was used, isolated from the liver of a child and about 1 year old. Two calves, 3 months and 3 weeks old respectively, received suspensions of the culture into the peritoneal cavity. In both only slight local nodules were produced, some resembling spontaneous tubercle, others tending towards granulation tissue. Two calves, 3 weeks and 2 months old respectively, were inoculated into the trachea. In one case the large local abscess in the muscles of the neck indicated a deposit there of much of the material destined for the lungs. In the liver and lungs a small number of minute tubercles, devoid of tubercle bacilli, were found. In the other calf lesions were absent. Thus, in spite of the immature age of these animals, the tubercle bacillus may be said to have had but a trifling local effect on them. The tests on guinea-pigs indicate a very attenuated culture. Three additional calves inoculated subcutaneously with sputum containing many tubercle bacilli showed lesions equally slight.

The defect of most of these tests is the absence of parallel experiments with bovine tubercle bacilli. Inasmuch as we do not yet know anything concerning the relative resistance of cattle to tuberculosis (p. 501) at different periods of life, nor the relative effect of cultivation on the bacilli and of different modes of inoculation, such parallel experiments are quite essential. Of these few experiments, Bollinger's is the only one which might be regarded as favoring the susceptibility of very young cattle to human bacilli. Even here the disease penetrated only to the mesenteric and retroperitoneal lymph glands.

A summary of the inoculation experiments made by the writer upon cattle have already been given. Here we need simply to report the most salient features. These are—

1. The purely local, restricted character of the lesions in cattle due to sputum bacilli. Lesions were not found beyond the place of deposit or in the lymphatic glands to which these are tributary, excepting in one animal (Sputum V culture). In this case we find a multiple tubercular focus measuring in toto about 1 to 1.5 cm. in one of the dorsal mediastinal glands. This is the only affected gland found in the 5 cases. Considering the fact that the bacillus was one of the more attenuated, that on the other

hand the animal was fully 4 years old, I am strongly inclined to look upon this isolated instance of lymph gland infection as a latent infection with bovine bacilli which was probably favored by the depressing effects of the injection into a slight activity. I take this ground because of its isolated occurrence and the very typical bovine character of the lesions. It is not unusual for such a slight lesion to be encountered in animals which have failed to react towards tuberculin, for experimenters agree upon a margin of error of 5 to 10 per cent, the lesions found in such cases being usually quite insignificant. Had the culture used not shown a virulence not only above but slightly below the average virulence of the other sputum bacilli, as tested on a rabbit and on guinea-pigs, the above inference could not be justly drawn.

2. The atypical tissue changes induced by the sputum bacilli which tended chiefly towards granulation tissue. Tubercle formation recognizable as such was uncommon. Besides the lymphatic focus cited above as of doubtful origin, tubercles approaching nearest the bovine type were encountered in the primary lung focus in the youngest animal (Sputum IV).

(p. 502) Some writers, including Bollinger and Baumgarten, are inclined to regard the pediculated masses produced on serous membranes by the inoculation of sputum or of cultures (Sputum IV, VI) as something specific and as deciding positively the transmissibility of human bacilli to cattle. Leaving aside the abortive, atypical, microscopic structure of the pediculated masses produced in the writer's series, and assuming that the inoculation of young calves may furnish lesions of a more typical character, we may present anatomical and histological facts which go far to show that there is nothing characteristic or peculiar about them or about pearly disease in general.

On the omentum and the pleura of cattle not tuberculous there may exist in many cases patches of delicate filamentous fringes, probably in all cases the result of some local inflammation. These fringes are microscopic in size and only visible to the naked eye when they are present in large numbers and congested. My attention was first called to them in the study of Texas fever. Owing to the congestion of the whole portal system, these fringes,



massed together, appeared as red patches on the omentum. The microscope showed them to consist of a capillary encased in a sheath of delicate fibrillar tissue and the latter covered by the endothelium of the peritoneum. Recently I have demonstrated the same fringes in slightly raised, reddened patches of the costal pleura in otherwise healthy cattle. Here they are quite inconspicuous, but may be demonstrated by seizing the surface of the membrane with delicate forceps. Invisible threads hold the latter near the membrane. In the fresh condition their structure is like that of the fringes on the omentum. In some I was unable to demonstrate a capillary. In all cases they consist of the wavy fibrillar tissue devoid of nuclei, but containing at times a few granule cells, recognized as acidophile leucocytes in stained sections. In sections, these fringes could be traced from their attachment to the serosa. The fibrillar tissue is directly continuous with the subserous layer of like tissue and the endothelial layer of the pleura is continuous over these fringes. The immediate union of fringes containing a capillary with the pleura was not demonstrated in the limited number of sections examined. Besides these of the simplest structure, others are seen in an active state of proliferation and infiltrated with lymphoid and acidophile leucocytes.

These fringes or filaments, probably the result of traumatic and other inflammation, form an excellent place of attachment for the injected tubercle bacilli. Here processes of epithelioid and giant-cell formation go (p. 503) on rapidly when bovine bacilli are present, whereas the sputum bacilli tend to lead only to granulation tissue, with slight abortive tubercle formation. These new formations, subject to pressure and friction, may undergo haemorrhage, anaemic necrosis due to twisting of the pedicle, and subsequent increase of the connective tissue stroma around the dead fringe. In this way those peculiar smooth nodes probably arise which are briefly described under the cases inoculated with Sputum cultures IV and VI. It is, furthermore, evident from the inoculation experiments that, among other causes, the tubercle bacillus itself is one inducing the formation of granulation tissue. The highly vascular, velvety layers of granulation tissue

carpeting the costal pleura in most of the cattle inoculated is a sufficient proof of the existence of this tendency. The pearly disease may thus be a product of at least two factors, the presence of this tissue as a result of former proliferation, and the inherent tendency of the serous membranes of cattle to respond by the formation of these vascular fringes to tubercles situated under the pleura and to bacilli discharged subsequently from such tubercles. But still other factors may be concerned.

That a certain retarded movement of the disease process may produce pearly disease in other animals have been answered in the affirmative for rabbits by Troje and Tangl.\* These authors inoculated subcutaneously bacilli from cultures and material from the tuberculous lungs of rabbits which had been intimately mixed with iodoform and kept in the dark in contact with it for one or two weeks. In two rabbits, from two separate experiments, chloroformed respectively 7 and 9 months after inoculation, pediculated tubercles of the serous membranes were found. Those not containing angular concretions, and therefore sectionable, were peculiar in the possession of a very large number of very large giant cells.

This observation I am able to confirm by one case, the rabbit inoculated with the culture of Sputum VI. This rabbit was chloroformed  $3\frac{1}{2}$  months after the intravenous injection of tubercle bacilli. Its weight had risen from 1304 to 2061 grms. The notes on this case are briefly as follows:

Organs apparently unaffected (brain and cord not examined), excepting the liver, kidney and lungs. The liver contains a small number of 1 to 2 mm. centrally caseous foci. The kidneys show a considerable number of grayish opaque 1 mm. tubercles. The lungs collapse well. They are everywhere beset with translucent bodies, seen with some difficulty, owing to their glassy (p. 504) appearance. Some have a minute, point-like, opaque centre. In the small cephalic lobes there are larger confluent patches, especially on the margins, of a peculiar grayish-translucent appearance. Sections of hardened tissue show the distinctly epithelioid character of the tubercular changes, with very few giant cells. Necrosis only in the largest foci. Tubercle bacilli

\* Deutsche med. Wochenschrift, 1892, 191.

fairly abundant in the necrosed centres, elsewhere scarce. From the marginal tubercles finger-like prolongations, precisely like those of the bovine pleura, project into the pleural cavity. They consist mainly of rapidly proliferating connective-tissue cells imbedded in a very delicately fibrillar meshwork. The basal portion of the fringe is partly covered with endothelium continuous with that of the pleura and contains a number of capillaries in transverse section. Similar vascular fringes appear on the opposite margin of the same section.

It is not improbable that if this animal had been allowed to live as long as those of Troje and Tangl, tubercle bacilli would have found their way into these fringes and produced the so-called pearly disease. This rabbit was allowed to live longer than any other of the sputum series. We may thus assume that neoplasms of the pleura in rabbits may be looked for after the third month. These observations go far to show that the eruption of tubercles on the pleura is not so much an expression of peculiarity on the part of the tubercle bacillus as it is an expression of a certain grade of virulence of the bacillus in an organism possessing a certain grade of resistance to it. To these conditions may possibly be added a pronounced tendency in certain animals towards production of granulation tissue of a certain type on serous membranes.

Troje\* has also described a rare case of pearly disease in man, affecting the pleura. Here, possibly, the previous existence of outgrowths like the fringes on the serous membranes of cattle may have been responsible for the peculiar localization of the tubercle bacillus.

Putting all the facts obtained by experiments upon cattle together, it would seem as though the sputum bacillus cannot gain lodgment in cattle through the ordinary channels. These avenues, well provided with protective mechanisms, receive the bacilli probably one at a time. However closely the sputum and the bovine bacillus may be related, it seems as if under ordinary circumstances the former would fall an easy prey to destruction. This inference will gain in weight if we bear in mind that the far more potent bovine bacillus produces in at (p. 505) least 50 per

\* Loc. cit.

cent of the spontaneously infected cattle a purely local disease, which probably would remain so if the animal were surrounded with favorable conditions.

The second and most important proposition, the transmission of bovine bacilli to the human subject, has been much discussed in recent years, without, however, bringing us any nearer to definite knowledge.

A recent compilation of cases of presumable transmission from cattle to men, both through wounds of the skin and through the digestive tract in milk, by Ravenel,\* gives perhaps the most condensed account up to date. To these may be added a most interesting case reported by Coppez.† A girl 17 years old had a wound on the palmar aspect of the third finger between the 2nd and 3rd phalanx, which became infected with tubercle bacilli during milking. The original lesions gave rise, within 6 months, to over 35 subcutaneous abscesses situated in different parts of the body. There were two on the right hand, four on the elbow, two on the shoulder-blade, several on the right cheek, two on the left palm, one on the back of the neck, a dozen on the buttocks and thighs, four on the left leg, three on the sole of one foot and one on the big toe. Most of these were curetted, and iodoform applied 6 months after the beginning of the disease. Subsequently more appeared, in all from 60 to 66. The author describes the appearance of these foci as follows:

At a certain point, always in the neighborhood of a preëxisting focus, a thickening of the subcutaneous tissue appeared, associated with increased heat of the skin and pain on pressure. The heat soon disappeared, and a fluctuating livid tumor opened itself and discharged pus and later a yellowish serum. These various abscesses healed slowly, and within a year all had disappeared. At no time could any visceral lesions be recognized, but one eye became involved. The nature of the affection was demonstrated by inserting some pus from an abscess into the eye of a rabbit. There was but slight reaction at first. Subse-

\* Journal of Compar. Medicine and Vet. Archives, December, 1897.

† Un cas de tuberculose cutanée et oculaire sans manifestations viscérales, Rev. gén. d'ophthalm., xv (1896), 433.

quently the whole eye became diseased, the lymph nodes of the neck being greatly enlarged. After several months death ensued.\*

(p. 506) If bovine bacilli may invade the human body without let or hindrance, we have not only food infection through milk and milk products to guard against, but also the inhalation disease to which men are exposed in stables containing tuberculous cattle. What proportion of tuberculous subjects may derive their infection from these sources we do not know. Now that we have established some fairly pronounced differences between bovine and sputum bacilli, the whole discussion might be cut short by the suggestion that the time has come to stop citing old and doubtful cases and to go to work to study with care the tubercle bacilli from cases of supposed animal origin, so that some experimental, trustworthy basis may be formed upon which to found statistics. While this is in truth what will have to be done and is the goal which has been aimed at from the outset in this tedious work, it will take much time and persistent attention to collect evidence of this kind. In the meantime the relation of bovine to human tuberculosis must be somehow defined before a fairly helpless and frightened public. It seems to me that, accepting the clinical evidence on hand, bovine tuberculosis may be transmitted to children when the body is overpowered by large number of bacilli, as in udder tuberculosis, or when certain

\* In an article written just before the discovery of the tubercle bacillus, Creighton (*Bovine tuberculosis in man*, *Journ. Anat. and Physiology*, xv (1880), 1-177) describes 12 cases, following one another quite closely in the same hospital, which he considers to be afflicted with the bovine disease. This type of tuberculosis was characterized by eruptions on the serous membranes, large, grayish-white medullary tumors in the lungs, frequently assuming the form of a wedge, and by certain microscopic peculiarities. These cases may have been due to some other organism. Quite recently Askanazy (*Ueber tumor-artiges Auftreten der Tuberkulose*, *Zeitschr. f. klin. Med.*, xxxii (1897), 360), besides giving a good bibliography, cites 2 cases in full in which the peculiar type of disease leads him to suggest their relation to pearly disease in cattle. These articles simply impress upon the reader that the true interpretation of such cases will remain obscure until the etiological agent has been studied. The variable character of the tissue reaction to the tubercle bacillus, according to the species, deprives the pathological study, taken alone, of any decisive value.

unknown favorable conditions exist.\* To prevent this from occurring, a rigid, periodic dairy inspection and the removal of all suspicious udder affections and all emaciated animals is as much as public health authorities can at present demand. Any measures beyond these belong to agriculture, with which the public health has no business to meddle, without endangering the chances of (p. 507) gaining authority to enforce its own necessary measures. If the evidence gained by pathology in the future should reveal a greater danger than is here assumed, the scientific basis of such evidence will, I think, force all additional measures needed. But for the student of etiology the problem does not end in the differentiation of varieties. It reaches out much farther than this and involves some puzzling questions. The most important one bears on the possible changes which the tubercle bacillus may undergo during its prolonged sojourn in the human body. I have already referred to one phase of this question in mentioning the saprophytic growth of the sputum bacillus in the affected lungs and necrotic tissue, as contrasted with its slight multiplication in living tissue, and with the generally slight multiplication of the bovine bacillus in the tissue of cattle. This question is a very complicated one, and nothing is easier than to reason in a circle about it, because of the entire absence of data. The first hypothesis to be considered is that which assumes the conversion of the bovine bacillus into the sputum bacillus in the human body. This hypothesis would deny us all possibility of utilizing different characters of tubercle bacilli in tracing their source. If the bovine variety may enter into the digestive tract as such, and after a more or less prolonged interval emerge from the secondarily affected lungs as the sputum variety, we may as well give up all further study of the tubercle bacillus. The accumulated evidence of bacteriology is opposed to this view. Nevertheless, it has been unwittingly assumed by Klebs, in considering intestinal infection with the bovine bacillus, as a common cause of tuberculosis.† As a support of the view that

\* Probably much the same as in glanders. The number of glandered horses in certain places is out of all proportion to the cases in men who are continually handling and cleaning them.

† Die kausale Behandlung der Tuberkulose, 1894, p. 34.

tubercle bacilli change but very slowly, I may again mention the inoculation test upon a rabbit of Bovine culture I. About three years after the first test, the second test resulted in only a very slight prolongation of the disease. The first rabbit succumbed in 17, the second in 22 days. It was thus after 3 years of artificial growth still far above sputum bacilli in pathogenic power.

The question of phthisis as secondary to infection by way of the digestive organs is, however, one needing more attention, for experimental (p. 508) results in this direction are quite suggestive. In all mammals the lungs are evidently the most favored place of tubercle bacilli, and wherever the latter may be deposited, they sooner or later, unless the disease is checked, reach that organ, where the process spreads more rapidly than elsewhere. This march from the place of infection is not infrequently partially concealed by reparative processes. A recent case in point is that of a guinea-pig inoculated with a culture of Sputum VI:

Aug. 29, 1897. Male guinea-pig, weight 420 grams. Receives subcutaneously in the flank 0.5 cc. of a clouded suspension of tubercle bacilli (Sputum VI) 9 days old.

Nov. 8. Breathing now labored; has been active since inoculation.

Nov. 11. Respiration labored and almost convulsive; hence chloroformed; weight 431 grams.

No ulcer at point of inoculation.

Kneefold glands of this side as large as peas, yellowish in color, consisting of a thin-walled sac and homogeneous contents, resembling thick cream. Kneefold glands of opposite side moderately enlarged, but without necrotic changes. The pelvic, renal, retrogastric and mesenteric glands enlarged slightly, but without necroses. Spleen small, shows grayish specks disseminated through it. Liver and kidneys appear normal. Two small tubercles on left testicle.

Lungs do not collapse. They feel firm everywhere. On section most of the lung tissue is consolidated, of a grayish-white color. No fluid expressible from air tubes. In sections of the lungs, the infiltration consists chiefly of epithelioid cells with smaller, more deeply stained nuclei intermingled or in patches. No necrosis. The liver was, through an oversight, not preserved. The spleen shows in each follicle a rarefied area occupied by epithelioid cells and a few tubercle bacilli. No necrosis.

In this susceptible animal the only lesions threatening life or even conspicuous were those in the lungs. Those in the spleen were slight, possibly stationary. The disintegrated superficial glands might have discharged outwardly later on and healed. This is but one of a number of cases I have observed in the past 10 years in which there was progression in the lungs with almost complete destruction of the (p. 509) organ and retrogression elsewhere, showing itself in the liver by shrinking and furrowing of the organ.\*

With the two facts before us that tubercle bacilli gravitate, as it were, towards the lungs in all the susceptible mammals, and that they may conceal their movements in the body quite effectually, we must regard infection through the digestive tract as a source of phthisis at least deserving more attention. The only question to interest us here is the relation of the bovine bacillus to this process. Only much painstaking work will enable us to learn whether the human body can produce such a great modification of the bovine bacillus or not.

Another more acceptable hypothesis concerning changes in the tubercle bacillus would assume a slow, continuous modification which in the past has developed the sputum variety on the one hand and the bovine variety on the other. The future may enable us to establish not only other varieties linked to certain animal species, but also varieties which produce slightly different forms of disease in man himself.† The saprophytic life of the sputum bacillus in phthisis may be the cause of a very slow downward descent of its invasive power, which in the course of one or more generations may become perceptible both to the bacteriologist and to the clinician, and express itself to the statistician in the gradually falling curve of tuberculosis, as shown by the vital statistics of the past 40 years.‡

\* This generalization has been recently emphasized by Spengler (*Ztschr. f. Hygiene*, xxvi (1897), 321) as follows: The retarded course of an inoculation tuberculosis expresses itself without exception in a (greater) prominence of the lung disease with simultaneous retardation of the liver and spleen affection.

† Recently I have been able to study cultures of tubercle bacilli from a rapidly progressive tuberculous gland of the neck in an adult. These bacilli are slightly less virulent than the sputum bacilli described.

‡ S. W. Abbott. *The Vital Statistics of Massachusetts*. Rep. of the State Board of Health for 1896, p. 787-8.



The outcome of such slow changes would lead to the establishment of numerous minor varieties because of the great opportunity which tubercle bacilli have in our congested, abnormal city life of selecting their variously predisposed victims. Thus the more attenuated varieties may find their invasion obstructed in the more vigorous, but not (p. 510) in children or certain predisposed individuals. It is needless for me to illustrate these possibilities still farther. They have their parallels in nature all about us. Only one practical suggestion may be made, in view of the probable discovery of minor varieties of human bacilli. Tuberculous patients should not be indiscriminately exposed to other tuberculous patients simply because both are affected with a disease which bears the same name.\*

A more exhaustive experimental study of the tubercle bacillus away from the many variable factors acting upon the human body, which will lead to a better standardizing of virulence or invasive power, may help these speculations to find some substantial basis. That much is still to be learned concerning the etiology is evident from the want of unanimity as regards the channels of infection. The views of Koch and his followers of the transmission of the infection in dust and spray would tend to favor the hypothesis of gradual attenuation and of the production of minor varieties. Baumgarten's hypothesis of the transmission of the tubercle bacillus from parent to child before birth implies the transmission of tubercle bacilli either in a continual struggle with living tissue or else remaining in situa-

\* A beginning in this comparative study of different clinical types of tuberculosis has been made by Auclair (*Arch. de méd. exp.* (1897), ix, 1124). This article, which came to my notice after the completion of this manuscript, describes 4 cultures, one from a rapidly progressive tuberculosis of a gland on the neck, one from a slow phthisis, one from an acute meningitis and one from true scrofula. On guinea-pigs the intra-abdominal inoculation of these cultures had nearly the same effect. Hence the author did not hesitate to regard them as identical in pathogenic power, in opposition to the views of Arloing, who considers the bacilli of phthisis and those of the surgical forms of tuberculosis of different virulence. Auclair did not inoculate rabbits, in spite of the fact that Arloing regarded them as the best means of differentiating the bacilli of the different forms of tuberculosis. My own results show that if the intra-abdominal inoculation of guinea-pigs is the only test made, practically no differences worth considering would appear between bovine and sputum bacilli, as regards pathogenic power.

tions where the bacilli cannot multiply, and hence where a tendency to loss of invasive power by saprophytic growth is impossible. The occasional entrance of bovine bacilli into the human body might open the way for the introduction of a virus of a higher level, provided opportunity for subsequent transmission be afforded (p. 511). If in this brief summary I have presented nothing but problems to be solved and doubts to be entertained, I feel quite confident that the comparative study of tubercle bacilli will lead to some definite understanding on certain important questions, and eventually to more light on the whole subject of tuberculosis from the preventive as well as the therapeutic side.

The main questions proposing themselves to the investigator are:

1. The study of tubercle bacilli from different types of tuberculosis to determine their relation to the sputum bacillus and the bovine bacillus as regards virulence.

2. The study of the bacilli in primary intestinal disease and in all tubercular disease in children in which the source of infection is assumed to be outside of the family and possibly in the milk.

In attacking these problems the investigator should either keep strictly to the methods suggested in this article, if he wishes to use its results as a basis, or else, in all cases in which the bovine bacillus or one of abnormal virulence is suspected, he should study fresh cultures of the sputum bacillus side by side with the other.



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SIR DOMINIC CORRIGAN (1802-1880)

(Courtesy of the Royal College of Physicians, Dublin. *Annals of Medical History*, 7, December, 1925)

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## Sir Dominic John Corrigan

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- 1802 December 1, born in Dublin. Received primary education at Lay College of Maynooth. Later, in same school, "engaged by Professor of Natural Philosophy to make experiments demonstrating the lectures, and it was from the practical knowledge of hydrostatics and pneumatics thus early acquired that he afterwards found such facility in demonstrating the diseases of the blood vessels as illustrated by changes in the circulation," Dublin Jour. Med. Sc., 69: 269, 1880. Apprenticed to the village doctor, Dr. O'Kelly, medical attendant at Maynooth College.
- 1825 Age 23. Graduated with M.D. from Edinburgh with William Stokes. Settled in Dublin and began work in association with Colles, Carmichael, Adams, Graves, Stokes and Collins.
- 1830 Age 28. Became physician to Jarvis Street Hospital where he had control of only six beds from which "he drew the most valuable portion of his clinical experience," and elaborated his article on aortic regurgitation.
- 1831 Age 29. Appointed consulting physician to Maynooth Catholic College.
- 1832 Age 30. Resided on Ormond Quay and was very active in treatment of cholera which appeared for first time in Dublin in virulent form.
- 1833 Age 31. Lecturer on Medicine in Carmicheal School.

- 1838 Age 36. Founder and subsequent President of Dublin Pathological Society. Succeeded Dr. Crampton as Physician to Whitworth and Hardwicke Hospitals.
- 1840 Age 38. Physician to House of Industry Hospital until 1866. Made Physician-in-ordinary to the Queen of Ireland.
- 1843 Age 41. Obtained diploma of M. R. C. S. (Eng.).
- 1847 Age 45. Appointed Honorary Physician-in-ordinary to Queen Victoria in Ireland.
- 1849 Age 47. University of Dublin conferred M.D. honoris causa.
- 1859 Age 57. Elected Fellow of Royal College of Physicians of Ireland.
- 1866 Age 64. Created a baronet.
- 1870 Age 68. Represented Dublin in House of Commons until 1874.
- 1871 Age 69. Selected Vice-Chancellor of Queen's University.
- 1875 Age 73. President of Pharmaceutical Society of Ireland.
- 1878 Age 76. Suffered slight paralytic stroke.
- 1880 Age 78. Died February 1, following a right hemiplegia of December 30, 1879.

Member of Royal Irish Academy.

Member of Academy of Medicine, Paris.

Member of Harveian Society, London.

President of Irish College of Physicians on five different occasions.

Member of Senate of Queen's University, Dublin, on its foundation and for many years represented it on general Medical Council of Britain.

Fine statue of Corrigan was presented by numerous friends and admirers to the College of Physicians of Ireland.

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CIRRHOSIS: Of the lungs. *On cirrhosis of the lungs.* Dublin Jour. Med. Sc., 13: 266-286, 1838.

DISEASE: Aortic incompetency or regurgitation; called "maladie de Corrigan" in France. *On permanent patency of the mouth*

of the aorta, or inadequacy of the aortic valves. *Edinburgh Med. & Surg. Jour.*, 37: 225-245, 1832.

**PULSE:** A jerky pulse with a full expansion, followed by a sudden collapse, occurring in aortic regurgitation; also called water-hammer pulse. See **DISEASE**.

**SIGN:** The expansile pulsation of aneurism. *Aneurism of the aorta; singular pulsation of the arteries, necessity of the employment of the stethoscope.* *Lancet*, 1: 586-590, 1829.

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Intestines, ulceration.....	44	1843
Ireland, charities in.....	37	1842
Ireland, cholera map of.....	107	1866
Jaundice.....	75	1856
Kidney diseases (also see Bright's disease)....	63	1854
Laryngitis.....	39	1842
Liver, cancer.....	53	1846
Liver, hardened.....	74	1855
Lunatic asylums.....	92	1860
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	100	1862
Lung, cirrhosis.....	16	1838
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Pericarditis.....	42	1842
	60	1850
Peritonitis, tubercular.....	66	1854
Phthisis.....	24	1841
Pica.....	93	1860
Pleuritis.....	46	1843
	47	1844
Plica polonica.....	11	1834
Pneumonia.....	29	1841
	32	1841
	52	1845
	76	1856

	Reference	Year
Pneumonic abscess.....	59	1850
Pneumothorax.....	105	1865
Poisoning, atropia and opium.....	69	1854
Poisoning, copper.....	67	1854
Porrigio.....	41	1842
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Pylorus, stricture.....	21	1840
Rectum, tumor.....	88	1858
Rheumatism, acute.....	19	1840
Rupia.....	11	1834
Scarlatina.....	30	1841
Small-pox.....	104	1865
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Spinal irritation.....	7	1831
Stethoscope.....	1	1829
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Syphilitic eruption.....	23	1840
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Tubercular cavity and pulmonary artery.....	27	1841
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Women in medicine.....	114	1875

## INTRODUCTION TO THE WRITINGS OF SIR DOMINIC JOHN CORRIGAN

Dominic John Corrigan was fortunate, after obtaining the M.D. degree from Edinburgh University in 1825, in becoming associated with such doctors in Dublin as Adams, Carmichael, Colles, Collins, Graves and Stokes. Six years previously Laennec had invented the stethoscope and published his book on auscultation. In those early years of practice Corrigan must have frequently discussed these topics with his associates. So we find him in 1829 publishing two papers on the heart. One paper is reproduced in its entirety on the following pages. This paper is entitled *Aneurism of the aorta; singular pulsation of the arteries, necessity of the employment of the stethoscope* and describes the expansile pulsation of an aneurism so well that the name Corrigan's sign has become attached to this finding.

Such work evidently helped win for him the position of physician to Jarvis Street Hospital where he had control of only six beds. Then in 1832, at the age of 30, Corrigan wrote a paper which has made his name famous in medical history, *On permanent patency of the mouth of the aorta or inadequacy of the aortic valves*.

A collapsing pulse, the chief sign of permanent patency of the mouth of the aorta, had been noted by W. Cooper in 1705 and by R. Vieussens in 1715; both men simply described a clinical fact and did not discover the underlying pathology. Likewise Thomas Hodgkin, taking an idea from Mr. C. Aston Key, in 1829 described this disease but his explanations of the clinical signs are ambiguous. Corrigan did not know of Hodgkin's paper but in a masterly manner, a model for all medical papers, fully described the clinical findings and the underlying pathology, and advanced the correct explanation of the altered heart sounds.

Corrigan's article of 1832, *On permanent patency of the mouth of the aorta or inadequacy of the aortic valves*, is accompanied by an excellent illustration showing several different pathologic processes in the aortic valves. The author is quick to give credit for the name of this condition to Dr. Elliotson whose term is preferable to the one Corrigan had originally intended. The paper then covers in an orderly manner the pathologic changes in the valves, general symptoms and signs, history and progress of the disease. A clear explanation of the visible pulsation of the arteries is given. An unusual feature is the confession that certain beliefs in the author's papers of 1829 were erroneous. Finally the paper of 1832 covers diagnosis, differential diagnosis and treatment of this condition.

The great French clinician, Armand Trousseau, first applied the name Corrigan's disease and the French to-day still use the term "maladie de Corrigan."



# Aneurism of the Aorta; Singular Pulsation of the Arteries, Necessity of the Employment of the Stethoscope

BY

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"Such, however, was the power of prejudice, that it is observed, by Harvey, that no physician, passed the age of forty, believed in his doctrine; and that his practice declined from the moment he published this ever-memorable discovery." *Medical Facts*, Vol. 1.

**M**ANY of the profession still view with scepticism the utility of the stethoscope, in ascertaining the exact nature of thoracic disease.

I shall not enter into any general discussion on the merits of the instrument. This is obvious, that those who use it have not only all the information to be derived from symptoms, history of the disease, &c., which its opponents enjoy; but that, in the instrument, they have a medium superadded through which to obtain additional knowledge, and they are thus enabled to come to the examination of thoracic disease, as it were, with increased powers

of mind. A single well-applied fact may carry conviction where reasoning will not. Among the cases of thoracic disease which have been under my care, one was so much in point, so well calculated to remove the (p. 587) scepticism above alluded to, at the same time that it enforced so strongly the necessity of employing the instrument, that I should be culpable were I to allow it to rest in silence.

Mr. J. D.—e, a builder, (Cole's Lane), called on me, for the first time, in the early part of June. His complaint commenced about four months before that period, with sense of oppression and straitness in his chest, succeeded by cough, occasionally convulsive; the cough and oppression of chest always relieved by mucous expectoration. He might, at that time, have been selected as a man presenting the very vigour of health, finely made, full in flesh, of a florid complexion, and active in his limbs. He was daily engaged at his ordinary business, which required much exertion; but for his teasing cough, and straitness of chest, he should not, he said, have known what an ailment was. After having tried, without avail, all the usual domestic remedies, he had recourse for advice to several eminent practitioners in the city, who did not use the stethoscope. When he came to me, his breast was covered with the marks of recent cupping, and, between his shoulders, the back was bare from a blister; he had been repeatedly bled. The obstinacy in resisting the exhibition of active remedies of what seemed, at first sight, an attack of simple bronchitis, attracted my attention. Questioning him closely, I found that he occasionally felt pain in the left side of his neck and left arm.

On stripping him, the first remarkable appearance that caught the eye, was a singular pulsation of all the arterial trunks of the upper part of the body. As his arms hung by his side, the whole tract of the branchial and carotid arteries was thrown out in strong relief, at each impulse of the heart, as if the vessels, from having been previously comparatively empty, had become suddenly filled. Mr. D. was above the middle size, well-formed, and his chest made fully, in proportion. On percussion, the thorax, with the exception of the part midway between the left mamma

and sternoclavicular articulation of the same side, sounded clear; in this situation, there was great dulness of sound. Respiration was pure, save in the same place, where, in its stead, existed a most intense "bruit de soufflet," accompanied by indistinct pulsation. The action of the heart was regular. Pulse about 80, full, equal, the same in both arms. He knew of no immediate cause to which to attribute his illness. About six months before its commencement, when assisting his men in removing some timber, one end of a long plank, from the opposite end of which the support had been suddenly pulled away, canted upwards, and, hitching under his sternum, tossed him into the air; he fainted, but soon recovered, was bled, and felt no further ill effects.

I requested to see him again at the end of ten or twelve days. I had scarcely a doubt as to the nature of the disease; but before giving an opinion which, in his apparent state of good health, would have been so great a shock to his friends and family, I was anxious to be positive of the accuracy of my diagnosis.

On the second visit, his symptoms were as before, but somewhat aggravated. On placing him sitting opposite a window, and looking from behind, aslant down his chest,\* there was a prominence, although very slight, perceptible above the left mamma, where the sound was dull, and the "bruit de soufflet" intense. I had now no doubt as to the nature of the disease, that there was aneurism of the ascending aorta, and that the termination must almost inevitably be fatal.

As I am relating this case partly to prove the absolute necessity of having recourse to the methods of examination of Auenbrugger and Laennec, in exploring diseases of the chest, I may pause here to meet the objections of those whose prejudices may make them disbelieve in, or scoff at, the stethoscope.

Such persons, in speaking of this case, would bring forward two objections to the instrument; first, that the disease could have been discovered without it, therefore that its application

\* This is a posture and mode of observing in which dilatation of the forepart of the chest is most easily ascertained by the eye.



was unnecessary; secondly, that supposing the disease to have been discovered by the use of the instrument, nothing was gained, inasmuch as the disease was fatal. To the first objection, instead of going into lengthened reasoning to prove that symptoms could not have guided to an infallible diagnosis, I shall merely reply, that until my examination of Mr. D., there was not the slightest suspicion entertained by his medical attendants of the nature of the disease. To this, perhaps, it will be answered, "The persons under whose care he had been were ignorant." Of those who were in attendance on him previous to me, two are men whose names, could I with propriety mention them, would be to this a sufficient answer; they stand at the very head of their profession. They brought to the investigation of the case, talent and experience, and they erred; I impute not the least blame to them; they did all that could be done with the means which they possessed. One (p. 588) of them I met more than once in consultation on this very case. With a candour that does him honour, he acknowledged to me that he had considered the case as bronchitis. To charge these gentlemen with ignorance, or for any one to say that, with only the same means of acquiring information, *he* would not have made the same mistake, would be arrogant presumption.

A trite objection frequently made to the stethoscope, and which those who put it would consider peculiarly applicable to this case, is the second.

Granting that the practical organic lesion were discovered by the stethoscope, the disease is inevitably fatal; what, then, is the use of the discovery? This is an objection that should never come from the lips of a man of science. In the pursuit of science every truth, every fact discovered, is of value. We may not, in every case, see its immediate application, or instant practical good result, but it is a step gained. We know not how soon it may become important, or whether, although yet unknown to us, it may but be the way to a hitherto unexplored field of knowledge. It is only for those of narrow minds to say, that facts, or means of attaining facts, should be disregarded, because there is not some immediate obvious practical result. In taking up the question

thus, I am, however, allowing the opponents of the stethoscope more than I ought; but I am willing to give them every advantage in the argument. I have supposed the disease in question to be fatal in every instance. It is not so. Some few, although few, cases are known of recovery; and while there exists a hope, no means should be left untried. It is scarcely necessary to say, that the chance for recovery depends altogether upon a plan of treatment quite opposite to that for almost every other thoracic disease. There is, then, gained, a just and steady practice, and an exclusion of plans of treatment which would almost certainly hasten death. Suppose, however, this particular disease *to be in every instance fatal*, is it nothing to abstain from torturing a patient with not alone inefficient, but positively injurious means? Is it nothing to foretell, and thus in some measure take from, the approaching calamity? Is it nothing, instead of giving delusive hope, to prepare the individual himself for his last great change, and that, in all probability, to be sudden? Are all these matters of little consideration? Had this patient, whose case I am recording, died (in making some exertion) from a rupture of the sac, which was most likely to happen, say but twelve hours previous to the examination with the stethoscope, should we not have had this added to the number on record of cases of internal aneurism ending in sudden death, without its having, during life, it would be asserted, presented any symptom by which to discover it?

I have made these observations merely as they arose out of a single case; I might go much further, but this is not the place. I shall now resume the details.

Pain, which had at first been trifling, increased in degree, occupying the left side of the chest, shooting out through the left scapula, extending down the arm and up the side of the neck, sometimes encircling the throat. The nights were restless, disturbed by harassing cough, followed by mucous expectoration. The prominence above the left mamma increased, although very very slowly, in projection, and the finger pressed on it detected the "*bruissement*" described by Corvisart as a symptom of aneurism of the ascending aorta. There was not, however, at

any period, the "*sifflement*" in the breathing, mentioned by the same author, as accompanying the disease. Vasalva's treatment was the only one that held out any prospect of relief. It was put in practice. Rest, abstinence, frequent bleedings, with the exhibition of digitalis, were employed. Digitalis was pushed to the extent of forty drops three times a day, with very little benefit. On many occasions the sufferings were often more distressing on a night succeeding the bleeding, than on any other. The digitalis at one time brought the pulse down to 48, but otherwise gave no relief. The pulse very soon rose again. The blood drawn was buffed and cupped, in every instance, with a firm coagulum. From the middle of June, to the 26th of August, when death took place, three symptoms were invariably present; remarkable pulsation of all the arteries of the superior extremities; loud "*bruit de soufflet*" in the ascending aorta and trunks branching from it; "*fremissement*" accompanying. It would not be instructive to follow up minutely this melancholy case. The pains shooting about the neck, chest and scapula, were sometimes most agonising. Leeches occasionally gave relief. Belladonna liniment, in the proportion of half an ounce of the extract to two ounces of water, sometimes afforded ease. This failed: then a plaster extract. belladonnae, emp. ammoniaci, and powdered opium, applied, after leeches, to the pained parts, alleviated the sufferings, but at last all failed. Towards the termination, the pains became so torturing as sometimes to deprive the patient of reason, and sense of horrible suffocation frequently came on at night, making him bound suddenly from bed, and fly to the open window for breath. Two days before death, the feet were edematous; pulse weak; skin of the entire body of varying shades of purple. Mucous and bloody stools were (p. 589) passed, and at length, without any expectoration of blood, death by suffocation closed the scene.

I examined the body 24 hours after death, in the presence of Doctors Harkan, Ferguson, Higgins, surgeons Adrien and Peebles. The abdominal viscera were sound; liver gorged with blood. The lungs were also gorged, but pervious through their whole extent, and perfectly sound in texture. Slight effusion in the pleurae;

three or four ounces of blood-colored serum in the pericardium. The heart was somewhat enlarged. The aorta, from its origin to its arch, was dilated to the size, at least, of a pint measure; from the arch the vessel was of natural size. There were two or three trifling cartilaginous deposits upon the descending aorta. The arteria innominata, carotid, and subclavian arteries, were of natural size, and sprung from the termination of the sac. The aneurism was in front, attached to the sternum, (on which there were marks of commencing absorption), and to the cartilages of the three superior ribs. Behind it compressed, between it and the trachea, the pulmonary artery, which was, in consequence, dilated at its origin. The cavity of the sac was filled with blood, coagulated after death. No appearance whatever of an attempt at coagulation during life. From the formation of the aneurism, this, indeed, could scarcely have been expected. The dilatation of the vessel was nearly equal all round, a little greater in front. It was not at all, however, in the form of a pouch on the side of the vessel. It presented, in the most satisfactory manner, all the characters of true aneurism. It was equally dilated, weak, thin, smooth on its internal surface, and the fibrous tunic could be distinctly traced over the entire sac. It showed distinctly the error of Scarpa's assertion of the non-existence of true aneurism. The walls of the dilated vessel were so slender, that it was a wonder rupture had not taken place. The tumour, by its bulk, had caused death, by pressing on the pulmonary artery, and thus impeding the circulation through the lungs. The exit of the blood from the right ventricle was obstructed; the return of blood in due quantity, from the general circulation to the right side of the heart, prevented. Venous congestion over the entire system, even in the lungs, was the effect. The subcutaneous effusion, effusion into the cavities, mucous and bloody stools, were the efforts of the system to relieve itself from this congestion. From the obstructed pulmonary circulation, imperfectly arterialized blood was distributed through the body. The brain suffered in its functions; hence constant dreaming, and very frequently delirium, occurred, particularly after sleep, when volition could not be exerted to assist by change

of posture the respiration and circulation. At length suffocation put an end to a miserable existence.

Laennec reckons aneurism of the aorta one of three thoracic affections, which still remain in obscurity, notwithstanding the application of the stethoscope.

It is singular, that among the symptoms given by Corvisart and Laennec, there is no mention of the visible pulsation of the arteries of the upper extremities, so remarkable in this case. Three cases of aneurism of the ascending aorta, or its arch, are in my recollection; in each of them this was a prominent symptom. Aneurism of the aorta is not a common disease. I can scarcely, therefore, suppose that this symptom should have existed in all the cases that occurred to me, yet not in any of those that came before Corvisart or Laennec, and I am forced to think that it must have escaped their notice. It will be found, I believe, a valuable pathognomonic sign of the disease. This peculiar appearance of the arteries is noted, for the first time that I am aware of, by the relator of a case of aneurism of the aorta, in Dr. Macleod's Journal, vol. ii. He cites it triumphantly, as a proof of the muscularity of arteries. To this we shall return.

Without having recourse to the assumption of a power of very problematical existence in the arterial tunic, to say the least, a simple law in hydrostatics will afford us a solution of the phenomenon.

Suppose an aneurism of the arch of the aorta; the pressure of the fluid on its internal surface will be as the area of the surface. The walls of the sac are not at all strong, in proportion to their extent. The same degree of strength that enables an artery, through its small diameter, to resist a distending force, is far from being sufficient for the sides of a cavity capable of containing a pint. The organic contractility of the arterial trunks, arising from the sac (or immediately by it) pressing the mass of fluid through the sides of the sac, and the mere hydrostatic pressure of the column of blood in the carotid, making, on the sides of the sac, a pressure, increasing, as their area, will cause a yielding in its sides, which does not take place in any other part of the arterial apparatus. Hence the arterial branches, the

subclavian, brachial, &c., will, from this disproportion in the resistance, become, in some degree, emptied of their contained blood, by pouring it back on the cavity of the aneurism, after each systole of the heart. If the carotid have the area of an eighth of an inch, and contain half an ounce of blood, it produces a pressure of half an ounce upon every eighth of an inch over the interior of the sac. If the internal surface of the sac present an area one hundred or two hundred times greater than (p. 590) that of the base of the carotid, the pressure on the sides of the sac will increase in the same proportion.

The distending power exerted by the column of blood in the carotid, on the sides of the sac, is permanent; and it may be said the sac will, therefore, be kept constantly at its full stretch, and cannot dilate and contract, which would be necessary, in order to cause the phenomenon described. Such would be the case; but there is another distending power, which is only momentary in its operation, namely, that arising from the organic contractility of the arterial trunks, which converts the sac into a bag, alternately dilating and contracting, in the following manner.

The blow of the left ventricle is quick, sending forward a certain quantity of blood. The sac cannot follow, *pari passu*, in its dilatation the quickness of the impulse. Hence the overplus of blood received so suddenly is sent forward, or, what is the same, sends forward a corresponding quantity into the arterial trunks. They are distended to their full calibre, as in the healthy arterial apparatus. This, however, is only momentary. Immediately the overplus has been sent into them, they, by their organic contractility or elasticity, react on it, and throw it on the sides of the sac, producing a dilatation of the sac equal to what would be produced by the pressure of a column of blood of a certain height; and pouring back, of course, at the same moment, on the cavity of the aneurism, a proportion of the blood received; thus producing in themselves a comparative emptiness, which could not occur in an arterial apparatus, to which such a reservoir was not appended. This pressure can only be exerted on the sides of the sac, as long as the overplus of blood remains; but the capillaries are open to receive it. It passes silently along into

them. The sac resumes its original dimensions partly by its own elasticity, and partly by the elasticity of the surrounding parts, as the lungs, &c., compressed with it. The arteries, which have thus become comparatively emptied, and the sac which had resumed its original dimensions, are then as before the action of the ventricle; the next blow of the heart filling again, for the moment, the semi-distended vessels, produces the phenomenon described.

What takes place in injecting a subject for the dissecting table, supports the explanation offered. The arteries are empty, and, of course, not at their full calibre, as in the living body. If the eye be kept on the situation of even comparatively minute branches at the moment when the injection is sent in, these vessels are seen thrown out in strong relief, presenting precisely the same appearance which the larger trunks present in a case of aneurism. The arteries in the dead body present it in a more marked degree, because they had been more emptied. None will say that muscularity is the cause of this sudden jerking out of the vessels, at the moment of injection, in the dead body; as little reason is there to assert that to such a cause is it attributable in the living.

It may be asked why (if the explanation offered here be correct) was there not pulsation of the arteries of the lower extremities? The pressure of a column of blood, such as that in the descending aorta, even in a lying posture, is always sufficient to keep its branches fully distended; not so in the upper half of the body, where, through the entire of some of the trunks, and a portion of others, the force of gravity and of pressure is in constant opposition to the current of the blood.

Whether this singular pulsation of the arteries be a constant accompaniment of aneurism of the ascending aorta, it will remain for further observation to ascertain; but from what I have seen, were a patient to be presented to me with this symptom, with constant "*bruit de soufflet*," and "*fremissement cataire*" in the larger trunks, I would not hesitate to pronounce on the case.

Were the aneurism false, with very thick parietes, half filled with coagulum, or in a situation where the surrounding parts

might afford firm support, the symptom would be less marked; but false aneurism of the aorta within the chest is of very rare occurrence; and from the proximity to the heart, coagulation to any extent, unless under very active treatment, is not likely to take place. From the relative anatomy of the aorta, firm support cannot be afforded. The value of the symptom is, therefore, considerably increased by the absence of causes which might obscure it.

Two phenomena, well known to the disciples of Laennec, "*bruit de soufflet*" and "*fremissement cataire*," constantly accompany the peculiar pulsation of the arteries. They have baffled inquiry as to their cause. It happened that I had many opportunities of observing them under varied circumstances. The present article has spun out so far, that I shall not enter into the consideration of them here, but reserve the result of my observations for another number.

Whether my observations and opinions be disproved or supported, I shall be equally satisfied. Truth is the prize aimed for; and, in the contest, there is at least this consolation, that all the competitors may share equally the good attained.

11, Upper Ormond Quay,

Jan. 1829.

P.S.—I may observe here, that the diseased parts, described above, are in my possession.

FINIS







*Fig. 2*



*Fig 3*



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PART I.

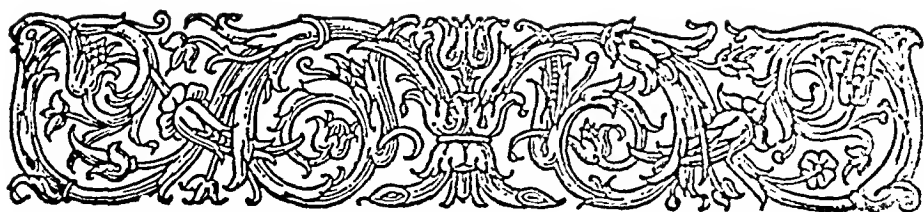
ORIGINAL COMMUNICATIONS.

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ART. I.—*On Permanent Patency of the Mouth of the Aorta, or Inadequacy of the Aortic Valves.* By D. J. CORRIGAN, M. D. one of the Physicians to the Charitable Infirmary, Jervis Street, Dublin; Lecturer on the Theory and Practice of Medicine; Consulting Physician to St Patrick's College, Maynooth.—(With Engravings.)

THE disease to which the above name is given has not, so far as I am aware, been described in any of the works on diseases of the heart. The object of the present paper is to supply that deficiency. The disease is not uncommon. It forms a considerable proportion of cases of deranged action of the heart, and it deserves attention from its peculiar signs, its progress, and its treatment. The pathological essence of the disease consists in inefficiency of the valvular apparatus at the mouth of the aorta, in consequence of which the blood sent into the aorta regurgitates into the ventricle. This regurgitation, and the signs by which it is denoted, are not necessarily connected with one particular change of structure in the valvular apparatus, and hence the name *Permanent Patency of the Mouth of the Aorta, or Inadequacy of the Aortic Valves*, has been chosen as simply expressing such a state of the parts as permits the regurgitation to occur.

VOL. XXXVII. No. 111.



# On Permanent Patency of the Mouth of the Aorta, or Inadequacy of the Aortic Valves

BY

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**T**HE disease to which the above name is given has not, so far as I am aware, been described in any of the works on diseases of the heart. The object of the present paper is to supply that deficiency. The disease is not uncommon. It forms a considerable proportion of cases of deranged action of the heart, and it deserves attention from its peculiar signs, its progress, and its treatment. The pathological essence of the disease consists in inefficiency of the valvular apparatus at the mouth of the aorta, in consequence of which the blood sent into the aorta regurgitates into the ventricle. This regurgitation, and the signs by which it is denoted, are not necessarily connected with one particular change of structure in the valvular apparatus, and hence the name *Permanent Patency of the Mouth of the Aorta, or Inadequacy of the Aortic Valves*, has been chosen as simply expressing such a state of the parts as permits the regurgitation to occur.

I have been in the habit for some years of describing this disease under the name of *Inadequacy of the Aortic Valves*; but as

Dr. Elliotson, in his elegantly written work on Diseases of the Heart, has given to a somewhat analogous morbid state of the auriculo-ventricular opening, a better name, *Permanent Patency*, I have, for that reason, and for the sake of uniformity, adopted the term, and I shall continue to use it as synonymous with my own term, *Inadequacy* of the Aortic Valves.

The morbid affections of the valves and aorta permitting this regurgitation are the following.

1st, The valves may be absorbed in patches, and thus become reticulated and present holes, through which the blood flows back into the ventricle.—*Vid.* Plate I. Fig. 1.

2d, One or more of the valves may be ruptured; the ruptured valves, when pressed, flapping back into the ventricle instead of catching and supporting the column of blood in the aorta, the blood then regurgitating through the space left by the broken valves.—*Vid.* Plate I. Fig. 2.

3d, The valves may be tightened or curled in against the sides of the aorta, so that they cannot spread across its mouth; and an opening is then left between the valves, in the centre of the vessel, through which the blood flows freely back into the ventricle.—*Vid.* Plate I. Fig. 3.

4th, The valves without any proper organic lesion may be rendered inadequate to their function by dilatation of the mouth of the aorta. The aorta, affected by aneurism, or dilated, as it frequently is in elderly persons, about its arch, will sometimes have the dilatation extending to the mouth of the vessel, and in such a case, the valves become inadequate to their function, not from any disease in themselves, but from the mouth of the aorta dilating to such a diameter, as to render the valves unable to meet in its centre; the blood then, as in the other instances, regurgitates freely into the ventricle.

Fig. 1. This figure scarcely needs any explanation.

It shows the reticulated valves.

The letters A, A, A, A, point out the openings produced by absorption in the valves, through which the blood regurgitated. These valves were very slightly thickened.

Fig. 2. A, points out the left-hand valve, with an opening

through it large enough to admit a goose quill, and ruptured from its connection with the aorta, so that it flapped back into the ventricle.

B. Bony depositions on the inner coat of the aorta.

C. The middle and right hand valves thickened, and contracted in their free edges, so that they could be separated only a very short distance from the sides of the aorta.

Fig. 3. A, A, Openings in the valves, as in Fig. 1, produced by absorption, one of the openings in the right hand valve large enough to permit the finger to pass through.

B. Middle valve, projecting downwards, curled back, and bound to the aorta by bony deposition, so that it was totally useless.

C. Bony deposition tying the edges of the middle and right hand valve together, and at the same time gluing them to the aorta.

*General Symptoms.*—On the general symptoms that accompany this disease, little is necessary to be said. Like most of those connected with affections of the respiratory and circulating organs, they are uncertain and unsatisfactory. There are frequently convulsive fits of coughing, more or less dyspnœa, sense of straitness and oppression across the chest, palpitations after exercise, sounds of rushing in the ears, and inability to lie down. Neither one nor all of these symptoms are essential to the disease. They may all arise from varied affections of the lungs, heart, liver, or nervous system. They neither tell us the seat of the disease, nor the extent of the danger.

*Signs.*—What is deficient in general symptoms from their obscurity, is, however, amply supplied by the certainty of the physical and stethoscopic signs, which may be referred to the three following indications. 1st, Visible pulsation of the arteries of the head and superior extremities. 2d, *Bruit de soufflet* in the ascending aorta, in the carotids, and subclavians. 3d, *Bruit de soufflet* and *fremissement*, or a peculiar rushing thrill felt by the finger, in the carotids and subclavians. In conjunction with these may be reckoned the pulse, which is invariably full. When a patient affected by the disease is stripped, the arterial trunks of

the head, neck, and superior extremities immediately catch the eye by their singular pulsation. At each diastole the subclavian, carotid, temporal, brachial, and in some cases even the palmar arteries, are suddenly thrown from their bed, bounding up under the skin. The pulsations of these arteries may be observed in a healthy person through a considerable portion of their tract, and become still more marked after exercise or exertion; but in the disease now under consideration, the degree to which the vessels are thrown out is excessive. Though a moment before unmarked, they are at each pulsation thrown out on the surface in the strongest relief. From its singular and striking appearance, the name of *visible pulsation* is given to this beating of the arteries. It is accompanied with *bruit de soufflet* in the ascending aorta, carotids, and subclavians; and in the carotids and subclavians, where they can be examined by the finger, there is felt *fremissement*, or the peculiar rushing thrill, accompanying with *bruit de soufflet* each diastole of these vessels. These three signs are so intimately connected with the pathological causes of the disease, and arise so directly from the mechanical inadequacy of the valves, that they afford unerring indications of the nature of the disease. In order to understand their value, it is necessary to consider their connection with the cause by which they are produced. The visible pulsation of the arteries of the neck, &c, may be first examined.

In the perfect state of the mechanism at the mouth of the aorta, the semilunar valves, immediately after each contraction of the ventricle, are thrown back across the mouth of the aorta by the pressure of the blood beyond them, and when adequate to their function of closing the mouth of this vessel, they retain in the aorta the blood sent in from the ventricle, thus keeping the aorta and larger vessels distended. These vessels consequently preserve nearly the same bulk during their systole and diastole. But when the semilunar valves, from any of the causes enumerated, become incapable of closing the mouth of the aorta, then after each contraction of the ventricle, a portion of the blood just sent into the aorta, greater or less, according to the degree of the inadequacy of the valves, returns back into the ventricle.

Hence the ascending aorta and arteries arising from it, pouring back a portion of their contained blood, become, after each contraction of the ventricle, flaccid\* or lessened in their diameter. While they are in this state, the ventricle again contracts and impels quickly into these vessels a quantity of blood, which suddenly and greatly dilates them. The *diastole* of these vessels is thus marked by so sudden and so great an increase of size as to present the visible pulsation which constitutes one of the signs of the disease.

That this visible pulsation of the arteries is owing to the mechanical cause here assigned is made evident by several circumstances. It is most distinct in the arteries of the head and neck, which empty themselves most easily into the aorta, and of course into the ventricle. In the arteries of the lower extremities, of even larger size than those which present it about the head and neck, it is not seen to any comparative degree, and most generally not at all while the patient is standing or sitting. It is much more marked in the arteries of the head and neck in the erect than in the horizontal posture; and a patient suffering under the disease himself, first pointed out a circumstance which is convincing of its being produced as asserted. He could increase the pulsation of the brachial and palmar arteries in a most striking degree by merely elevating his arms to a perpendicular position above his head. He thus enabled the brachial and palmar arteries to empty themselves more easily back upon the aorta. They became more flaccid, and then, on the next contraction of the ventricle, their diastole became comparatively greater, and their visible pulsation of course more marked. The same effect could be produced in the arteries of the lower extremities by lying down and elevating the legs on an inclined plane. The strength of the heart has little to do in producing this singular pulsation, for it is never observed in an equal degree,

\* It may be objected to the phrase *flaccid*, that the arteries, being capable of contracting upon whatever quantity of blood they may contain, are never flaccid. In using the phrase, it is not meant that the sides of the arteries, like a collapsed vein, fall together, but merely that, having become emptied of some of their blood, in consequence of its regurgitation into the ventricle, they are, while in this state, less tense than when at the next diastole they are distended by a fresh supply of blood to their limit of extension.



and most generally not at all, in the arteries of the lower extremities.

If it be asked, is the explanation here adduced of the cause of this visible pulsation sufficient to account for its appearance in the brachial and radial arteries, since the blood to return back from these vessels into the arch of the aorta should flow upward when the patient holds his arms in the ordinary position, flexed or hanging by his side? the following reply may be made. When the subclavians are pouring back their blood into the arch of the aorta and ventricle, the elasticity of the brachial arteries, acting upon the blood just urged into them, forces it back along with the retrograde current of the subclavians, no obstacle meeting it in that direction. The brachial arteries thus partially empty themselves, and become in their systole of a lessened diameter like the carotids and subclavians, but in less degree. The next jet of blood from the ventricle dilates them, and as in the subclavians, produces in them a visible pulsation: and if they be assisted in returning their blood by elevating the arms to a perpendicular position, their pulsation becomes, as has been already observed, much more strongly marked. The arteries of the lower extremities are not similarly circumstanced. The arteries of the upper extremities are assisted in emptying themselves back towards the heart, by the retrograde current in the subclavians and ascending aorta; but on the blood contained in the arteries of the lower extremities, the tall column of blood in the descending aorta is pressing, and prevents any return; or if it be supposed that of the large mass of blood in the descending aorta, a small portion flows back into the arch, it can produce little change in the contents of the iliacs and femorals; and moreover, whether the column of blood in the aorta be lessened or not in diameter, the pressure on the contained blood of the iliacs and femorals will remain the same, and keep these vessels distended. If we, however, as already observed, after the relation of the several arteries to the arch of the aorta, so as to facilitate the reflux of their contained blood, for instance from the radial arteries, by raising the arms to a perpendicular line above the head, from the iliacs and femorals, by placing the patient in

a recumbent posture, and raising the legs upwards on an inclined plane, the visible pulsation becomes much more marked in these respective arteries.

The *bruit de soufflet*, which is heard in the ascending aorta, carotids, and subclavians, with the accompanying *fremissement* in the latter arteries, is next to be considered. The *bruit de soufflet* characterizing this disease, is heard, as already observed, in the ascending aorta, its arch, and in the carotids and subclavians. It can be followed upwards from the fourth rib along the course of the aorta, increasing in loudness as it ascends, until it is heard of great intensity at the upper part of the sternum, where the arch of the aorta most nearly approaches this bone, and then branching to the right and left, it can be traced into the carotids and subclavians of both sides; and in these trunks it assumes a harshness that it did not possess in the aorta. This *bruit de soufflet* is synchronous with the visible pulsation, with the diastole of the arteries. It is no consequence whether the ascending aorta and its large branches be sound or be diseased; the *bruit de soufflet* is as loud in the one case as in the other. To account for the presence of this sign, and why it extends so far from the seat of the disease and along sound vessels, it is necessary to refer to a paper published in the *Lancet* of 1829, Vol. ii, p. 1. Continued observations from the date of that paper to the present, have confirmed the view then taken of the cause of that singular sound; of its being dependent purely on a physical cause, on a mechanical change in the manner of the blood's flowing.

In that paper is related an experiment, which it may be well to recapitulate here. A flexible tube, such as a piece of small intestine, or a portion of artery, is connected by one end with a tube which has a current of water of considerable force running through it. While the piece of intestine or artery is kept fully distended by the supply of water from the tube, no sound is produced by the motion of the fluid; but if the flexible tube, while the fluid is moving through it, be pressed upon in any part, so that the quantity of fluid passing through the contracted part is no longer sufficient to keep the further portion of the tube tense, then, beyond the contracted part, where the tube is less

tense, or in some degree flaccid, a distinct, and, according to the velocity or force of the current, a loud *bruit de soufflet* is heard; and, at the same time, if the finger be gently laid upon the part of the tube where the *bruit de soufflet* is heard, a slight trembling of the tube is perceived, evidently arising from the vibrations into which the current within is throwing its sides. If, in place of constricting any one part of the flexible tube, the whole tract of tube be allowed to become partially flaccid, by diminishing the supply of fluid, and the fluid be then allowed to rush along the tube by jets, at each jet the tube is suddenly distended, resembling the visible pulsation described above; and with each diastole of the tube, there is a sudden and loud *bruit de soufflet*; and, synchronous with the *bruit de soufflet*, there is *fremissement* felt by the finger.

Both the sound heard and the sensation felt by the finger in this experiment may be explained by the principles which regulate the motion of fluids. It may be remarked, that it is a property of fluid in motion, that, when discharging itself from the orifice of a tube into open space, or into a vessel of wider capacity not fully distended, its particles move in lines from the orifice, like so many *radii* tending to leave vacuums between them. When the flexible tube, artery, or intestine, therefore, is kept fully distended, the fluid moves forward as a mass, there is no tendency in its particles to separate from one another,—they all press equally,—there is no vibratory motion of the sides of the tube, and consequently no sound, and no *fremissement* or trembling. But if the tube be not kept fully distended, then the fluid propelled through it rushes along as a current; and its particles tending to leave vacuums between them, throw the sides of the tube into vibrations, which can be very distinctly felt by the finger, and which give to the ear the peculiar sound *bruit de soufflet*, and to the touch *fremissement*.

These principles may be applied to the state of the ascending aorta and its branches in the instances before us. When the aortic valves are fully adequate to their function of perfectly closing the mouth of the aorta, and thus preventing any regurgitation of blood, the aorta and its branches are kept fully distended, the blood is at each contraction of the ventricle pro-

pelled forward *en masse*, and there is no trembling, or vibratory motion of the sides of the aorta, carotids, and subclavians, and, as in the flexible tube when fully distended, no sound is emitted. But when the valves, becoming inadequate to their office, permit some of the blood contained in the ascending aorta, carotids, and subclavians, to return into the left ventricle after each contraction, then the aorta and these trunks become, like the flexible tube in the second part of the experiment, partially flaccid; and at the next contraction of the ventricle, the blood propelled into them is sent along as a rushing current, which throws the sides of these arteries into vibrations, and these vibrations give to the ear *bruit de soufflet*, and to the finger *fremissement*. These two signs may be traced to a varying distance from the mouth of the aorta, and always along the carotids, and to the outer third of the subclavians, and sometimes in the brachial arteries, as far as the bend of the arms, the distance to which they are heard being determined by the limit to which the current-like motion of the blood producing them is extended. In those cases in which the deficiency of the valves is considerable, allowing a full stream of blood to rush back into the ventricle, there is heard in the ascending aorta a double *bruit*; the first accompanying the *diastole* of the artery, the second immediately succeeding; and, in listening to the two sounds constituting this double *bruit de soufflet*, the impression made distinctly on the ear is, that the first sound is from a rushing of blood up the aorta, the second from a rushing of it back into the ventricle. It is impossible for those who have not heard this double *bruit* to conceive the distinctness with which the impression described is made on the ear. A patient in one instance heard this double sound distinctly in his own person, and referred it to its cause, a rushing of blood *from* and *to* the heart. The *bruit de soufflet* and *fremissement* are not perceived in the arteries of the lower extremities, when the patient is in a sitting or standing posture. The pressure of the blood in the abdominal aorta is sufficient in these postures to keep the vessels arising from it fully distended; and thus no vibratory motion of their parietes being permitted, there is no bellows sound, nor *fremissement* or rushing thrill.

*History and Progress of the Disease.*—Of eleven cases of the

disease, only two occurred in females, and in both of these the valves were nearly quite sound in texture; but the aorta being thinned and dilated, the valves could not meet so as to prevent regurgitation. None of the cases occurred in very early age. The youngest person presented labouring under the disease was twenty years of age. In this respect, inadequacy of the aortic valves differs from narrowing of the left auriculo-ventricular opening, which is not unfrequently met with in children, and even in infants at the breast. The causes of the disease are uncertain. In one case the disease followed an attack of acute rheumatism, which had been accompanied with symptoms of *pericarditis*. In some cases the commencement of the disease was referred by the patient to an inflammatory affection of the chest, which had occurred months or years before; while in others no cause or date could be assigned.

The symptoms accompanying its commencement and progress are very variable. Most generally the patient describes the first sensations as having been a feeling of oppression and straitness across the chest, with palpitation of the heart on any unusual exercise. These symptoms become gradually more distressing, and are after a very uncertain period of time accompanied by fits of coughing resembling paroxysms of asthma, and terminating in scanty expectoration. In a few cases, however, cough was not at any time, even up to the last hours of life, an urgent symptom; the oppression and straitness of the chest, with palpitation on any exertion, and an anxiety for a supply of fresh air, being the principal complaints. As the disease proceeds, the straitness and oppression about the chest become more distressing; fits of coughing more frequent; and the patient has an anxiety, approaching to agony, for a free supply of fresh air, frequently starting from bed at night under the dread of suffocation. In the last stage the state of suffering is extreme. The patient will not lie down for a moment from the dread of suffocation. The face, which had been pale, becomes purple on the lips as in suffocative catarrh; œdema of the legs comes on, followed ultimately by œdema of the hands and arms; there is no sleep, or there are almost incessant startings from it; the countenance assumes a most painful expression of sinking; and the patient at

length dies exhausted. The pulse in no case was under eighty. It ranged from that to 110; and in every case it has been all through the disease (unless influenced by medicine) full and vibrating, even to within a few hours of death. In the course of the disease, the superficial branches of the carotids, the brachial arteries, the radial, and the ulnar, and their branches, wherever near enough to the surface to be traced, become apparently enlarged, and remarkably tortuous;—the brachial artery in parts of its course often almost doubling upon itself. The *fremissement*, or rushing thrill, described as easily felt in the subclavians and carotids, can sometimes be felt by moderate tact as fast as the pulse in the wrist. The heart in all the cases that occurred was enormously enlarged, and its bulk arose from the state of the left ventricle, which in some cases was so much enlarged in cavity and in thickness, as to make the organ resemble rather the heart of a bullock than that of a man. The other parts of the heart, although necessarily obliged to keep pace in some measure with this increased size, did not at all partake equally in the enlarged bulk. The impulse of the heart was far less than natural, even in cases where the hypertrophy of the left ventricle was greatest. In some of them no impulse could be felt; and in none did the impulse during life give at all a proportional measure of the excessive hypertrophy discovered after death.\*

\* Laennec has stated, and his assertion is supported by many, that the degree of impulse is always a correct index of the degree of hypertrophy of the ventricle, but it is now admitted by some most capable of judging, that the impulse of the heart is not to be considered a gauge of the hypertrophy of the ventricle. Andral, in his "*Clinique Médicale*," Vol. ii, p. 160, says "Plus d'une fois dans des cas où après la mort nous avons trouvé les parois des ventricules très épaissies en même temps que leurs cavités étaient notablement agrandies, nous n'avions reconnu pendant la vie aucune espèce d'impulsion. Dans d'autres cas, où il y avoit simple hypertrophie du ventricule gauche, avec grande diminution de sa cavité (hypertrophie concentrique de MM. Bertin et Bouillaud,) il n'y avoit pas eu non plus d'impulsion appreciable." Piorry (sur la Percussion, p. 139) says, that impulse of the heart, carried even to raise the head of the observer, is far from being a constant sign of hypertrophy. Dr. Graves, in a clinical lecture, (*vid. Med. Gazette*, March 1831, p. 714,) says, "I can assert in the most positive manner, that I have seen cases of pneumonia in which the heart's pulsation continued violent until within a short time of dissolution; so much so indeed, as to induce the erroneous belief in myself and other medical attendants, that this organ was in a state of hypertrophy and dilatation, and yet it was found after death to be in every respect healthy." This subject will be resumed at another time.

Hæmoptysis very rarely occurs in the course of the disease, and the lungs are generally found after death permeable to air, and remarkably healthy. This is owing to the sound state of the auriculo-ventricular opening, and of its valves. This opening being full sized, permits the blood to pass with freedom into the ventricle, where it is retained by the sound auriculo-ventricular valves; and thus those sudden congestions of the blood-vessels of the lungs, so common in narrowing of the left auriculo-ventricular opening, are remarkably rare. The manner of death in inadequacy of the aortic valves is different from that in narrowing of the auriculo-ventricular opening. In the latter, owing to the obstacle presented by the narrowed opening to the passage of blood into the ventricle, the lungs are by any slight exciting cause suddenly congested; and the patient dies, not from the direct effect of the organic affection of the heart, but from the superinduced affection of the lungs,—pulmonary apoplexy, pneumonia, or suffocative catarrh. In the disease under consideration, the patient appears to die of mere exhaustion. The inefficiency of the valves of the aorta throws a great increase of labour on the left ventricle. The muscular energy of this part of the heart is in the course of time worn out. The heart is at length incapable of sustaining the column of blood incessantly pressing upon it; it ceases to contract, and is found after death largely distended with blood. The symptoms preceding death are in accordance with this state. For some days, or even weeks, before death, nature appears to be struggling against overwhelming exhaustion. The patient is constantly in the most heart-rending tone imploring to be relieved of the weight that is upon him; the countenance expresses the greatest sinking and distress; there are anxious calls for fresh air, and a continual restlessness, similar to what is seen in a patient sinking from hemorrhage; and when in this state the patient in some trifling motion dies exhausted.

The duration of this disease is very uncertain. No case was of less duration than two or three years, and some of the cases at present under treatment have been of seven or eight years standing. The time during which the disease may continue

without terminating fatally, seems to depend principally upon the extent to which regurgitation is permitted. The cases in which the valves, from small perforations, allowed but little regurgitation, continued for many years; while the case which furnished the Plate No. II. and in which the valves were ruptured and much injured, allowing considerable regurgitation, terminated fatally in less than three years.

*Diagnosis.*—Inadequacy of the aortic valves may be confounded with narrowing of the mouth of the aorta, either congenital or from diseased valves, with disease of the auriculo-ventricular valves, with aneurism of the arch of the aorta or *arteria innominata*, with nervous palpitations, and with asthma. Congenital narrowing of the mouth of the aorta is a very rare disease, but narrowing of the mouth of this vessel produced by vegetations on the valves is not unusual; and *bruit de soufflet* is a sign common to it, and to the disease we are considering. The resemblance between the signs of the two diseases extends, however, no farther. The visible pulsation of the arteries, arising from the arch of the aorta, which forms so striking a sign of inadequacy of the aortic valves, is wanting in narrowing of the mouth of the aorta. The pulse also is strikingly different in the two diseases. In narrowing of the aortic orifice it is small and contracted; in inadequacy of the aortic valves it is invariably full and swelling. In narrowing of the aortic orifice there is generally a marked contrast between the pulse and the impulse of the heart. The pulse is small and contracted; the impulse of the heart is strong and energetic. In the disease we are considering, when there is a contrast it is always in the inverse way; for while the arteries beat with violence, and the pulse is strong and full, the impulse of the heart is scarcely perceptible. When the mitral valves, becoming indurated or ossified, produce narrowing of the auriculo-ventricular opening, that narrowing produces *bruit de soufflet*;<sup>\*</sup> and the *bruit de soufflet* thus produced might be

<sup>\*</sup> The principles regulating the motion of fluids, already laid down, explain the production of *bruit de soufflet* in narrowed auriculo-ventricular opening. The blood at each contraction of the auricle discharges itself from a narrow orifice into the ventricle, "a vessel of wider capacity not fully distended."—"The particles" of the blood "move in lines



confounded with that accompanying inadequacy of the aortic valves. Independently of the visible pulsation of the arteries, and the state of the pulse, which accompany inadequacy of the aortic valves, stethoscopic examination points out with certainty the distinction of the two diseases. When the *bruit de soufflet*, is produced by narrowing of the auriculo-ventricular opening it is heard loudest just where the impulse of the heart against the side is felt; it comes with the impulse, and if loud it seems to rush into the ear; and as the stethoscope is removed from this point upwards along the sternum, it is heard growing fainter the farther the point of examination is from the point where the impulse is felt. In inadequacy of the aortic valves, the converse holds. For over the point where the impulse is or should be felt, *bruit de soufflet* is either not heard at all, or heard very indistinctly; but as the stethoscope is moved upwards from the heart, in a line corresponding with the ascending aorta, the *bruit de soufflet* is heard growing louder and louder, until over the arch of the aorta, and in the large trunks arising from it, the sound grates upon the ear with harshness.

Permanent patency of the mouth of the aorta may be mistaken for aneurism. If the arch of the aorta and *arteria innominata* approach more nearly than usual to the notch of the sternum, the visible pulsation at the root of the neck becomes so prominent, as to lead to a supposition that there is aneurism, and even of considerable size at this part.

Very lately a case came under my observation, in which there was a remarkable resemblance to aneurism. So strong were the pulsations for years in the region of the *arteria innominata*, that until the examination after death there was never even a doubt expressed that the case was not aneurism. The aorta was thinned, and was dilated so much as to render the valves inadequate to their office, and leave a permanent patency be-

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from the orifice, like so many radii tending to leave vacuum between them." This motion, as in the experiment of the tube, throws the sides of the ventricle into vibrations, which produce on the ear *bruit de soufflet*, and if the heart thus affected come forward so as to transmit through the parietes of the chest this vibrating motion, the hand laid over the heart perceives a *fremissement*, or trembling in the organ, the *bruissement* of Corvisart.

tween them. The *arteria innominata*, the carotids, and subclavians, were also dilated beyond their natural size, thus increasing the appearance of the pulsation, but there was no trace whatever of aneurism in the *arteria innominata*, such as had been supposed to exist there during life. An acquaintance with the disease under consideration, and a knowledge of the fact, that a violent throbbing at the root of the neck, or notch of the sternum, may arise from another cause than aneurism, will prevent the forming of a rash opinion on the cause of the violent throbbing. This throbbing may proceed from aneurism, or may arise from inadequacy of the aortic valves. When it proceeds from aneurism of the arch, or of the *arteria innominata*, it is confined to the vessel or the region of the vessel affected; the other trunks arising from the arch present only their natural, or even a diminished pulsation, and there is in the trunks arising from the arch neither *bruit de soufflet* nor *fremissement*. On the contrary, when the throbbing at the notch of the *sternum*, or in the region of the *arteria innominata* is from inadequate aortic valves, all the larger trunks arising from the arch pulsate in an equal degree, or with trifling differences, arising merely from the relative sizes of the vessels, or their relation to the surface, and they are never at any time without *bruit de soufflet* and *fremissement*.

Not only in relation to treatment, but in regard to the patient's mental anxiety, it is of importance to be aware, that inadequacy of the aortic valves may, by this violent pulsation at the root of the neck, closely simulate aneurism of the arch of the aorta, or the root of the *arteria innominata*. In aneurism of the aorta life is not for a moment secure, and it may be necessary that even for a remote hope of cure the patient should totally abstain from all exertion. In permanent patency of the mouth of the aorta the fatal result is never sudden; and under proper restriction the patient is not only able to lead an active life for years, but is actually benefited by doing so.

The two diseases, aneurism of the aorta, and inadequacy of the valves, may, however, be combined. Aneurism of the ascending aorta may, by extending to the mouth of this vessel, dilate it so, that the valves are unable to meet, and there is then a

combination of the two diseases; there is aneurism and there is permanent patency of the aortic opening. The first cases that came under my observation presenting the signs of inadequacy of the aortic valves were cases in which the valves were rendered useless in this way, namely, by the mouth of the aorta sharing in the aneurismal dilatation. These cases led me into an error; for, meeting the signs of permanent patency of the aortic orifice in conjunction with aneurism, I erroneously attributed to the aneurism the signs which arose from the permanent patency.\* Aneurism of the aorta of itself does not produce the signs arising from permanent patency of the mouth of the aorta. It can only produce them in the way already described, by involving in the dilatation the mouth of the aorta; and hence, when in conjunction with an aneurismal tumour of the *arteria innominata* or aorta, there are found visible pulsation, *bruit de soufflet*, and *fremissement* in the ascending aorta, and the trunks arising from it, we may be certain, that, in addition to the aneurism, there is a defect in the aortic valves, or that the aneurism has extended downwards, involving the mouth of the aorta. On the other hand, if these signs be absent, the valves are sound, and the mouth of the aorta is not included in the disease. The propriety of performing Mr. Wardrop's, or indeed the common operation for aneurism about the neck, might depend on the information thus acquired of the state of the aortic valves. To perform either in a case where the aneurismal dilatation was so extensive as to involve the mouth of the aorta, or where the aortic valves were diseased, would only bring the surgical treatment of the disease into unmerited discredit.

Palpitation of the larger arterial trunks, depending on derangements of the nervous system, will sometimes in their violence simulate the visible pulsation arising from inadequate aortic valves; and in females these palpitations will last not only for months but for years, and seem to justify an opinion that there is organic disease of the heart. This nervous palpitation is not, however, accompanied by *bruit de soufflet* and *fremissement*;

\* *Vide* Lancet for February 7th 1829.

and the absence of these two signs is conclusive as to the nature of the disease. Sometimes, however, more than one examination is required before pronouncing a positive opinion; for in a nervous patient, the alarm excited by the first examination will render the circulation hurried and irregular, and hence there may be in the carotid or subclavian a momentary *bruit de soufflet*. In making the examination it is moreover necessary, that the edge of the stethoscope should not be allowed to press on the artery, because its pressure is sometimes sufficient in those cases to produce the sound. When the *bruit de soufflet* and *fremissement* are only momentary, no value should be attached to them. In permanent patency of the aorta they are never absent. The convulsive fits of coughing ending in difficult mucous expectoration have made some cases of this disease be mistaken for asthma, and the state of the pulse has served to maintain the error; for the pulse being remarkably full, as it always is in the disease we are considering, seemed to be sufficient evidence that there was in the heart no obstruction to the circulation; hence the convulsive fits of coughing were supposed to have their origin in the lungs. With a knowledge of the signs afforded by the disease, no one of even moderate acquaintance with the stethoscope can confound it with asthma; without a knowledge of the stethoscope it will, however, be impossible in very many instances to distinguish between the two diseases. General symptoms will give no information on which the slightest reliance can be placed.

*Treatment.*—There is no class of diseases to which the scientific principles that guide modern medicine have been less applied than to diseases of the heart. From its curious mechanism, from the varied derangements to which that mechanism is subject, from the number of tissues that enter into its formation, and from its numerous sympathies, its diseases frequently demand most opposite lines of treatment; and yet it would seem, from the perusal of works on the subject, that one principle were thought sufficient for guiding the treatment of nearly all the diseases of this important organ. With the idea of heart disease, is too frequently associated the notion that such disease, without regard to its precise nature or its cause, requires the action and

continued enforcement of measures calculated to exhaust strength and depress vital energy; and this error is sanctioned by the standard works on the treatment of heart disease.

Corvisart says, that "in a great number of organic lesions of the heart, as, for example, in active aneurism, the indication is to diminish the general strength of the patient, and that of the heart in particular." Laennec, p. 739, says, that "though we cannot remove indurations of the valves and narrowing of their openings, we are nevertheless in such cases to follow up the same measures, (bleeding and starving) to remove or diminish hypertrophy:" and Bertin, p. 233, states that "the treatment of valvular alterations is to consist of general and local bleedings, of low diet, of preparations of digitalis," &c.; and p. 367, "that the measures to be employed against hypertrophy are to be essentially antiphlogistic, and calculated to produce debility." A little reflection on the nature of the disease now before us will show that these principles are inapplicable both to the treatment of the valvular alterations, and of the hypertrophy of the left ventricle, which accompanies that alteration.

The disease we are considering is an inadequacy in the valvular apparatus at the mouth of the aorta permitting a regurgitation of blood into the ventricle. In the perfect state of the valvular apparatus at the mouth of the aorta, the valves support by intervals the column of blood in the aorta, and the heart with its ordinary complement of fibre and of muscular strength, is with this assistance competent to the office it has to perform. But when, in consequence of a deficiency in the valvular apparatus, the heart does not receive its due share of assistance from these valves, and is obliged to perform not only its own function of propelling the blood, but has in addition to support after each contraction a portion of that weight of blood which should then be wholly supported by the valves, it is no longer in its ordinary state equal to the task imposed upon it. In such circumstances, nature, to enable the heart to perform the additional labour thrown on it, increases its strength by an addition of muscular fibre, and the heart thus becomes hypertrophied, in accordance with the general law, that muscular fibres become thickened

and strengthened when there is additional power required from it. Is this hypertrophy disease, or is it a wise provision of nature, by which the organ is thus made equal to the increased labour it has to perform? On the answer depends the treatment to be adopted; and on this there is no room for hesitation. A heart of ordinary strength could not, under the circumstances, carry on the circulation; and nature then wisely endows the heart with the requisite degree of strength. It is at once obvious that to interfere with this wise provision of nature, to diminish the strength of the heart, or, if we choose other words, to direct, according to the advice of Laennec, Bertin, &c. our measures against the hypertrophy of the organ, is to deprive the system of the only power which enables the heart to carry on the circulation. No one thinks of directing measures to diminish hypertrophy of the muscular tissue of the stomach, in narrowing of the pylorus from scirrhus of the bladder or rectum in stricture of the urethra or intestines.

In these instances the hypertrophy is recognized as a provision of nature to make the power of the part equal to the obstacle it has to overcome; and yet this simple principle seems to have been entirely overlooked in diseases of the heart, as if this organ possessed muscular fibres of a different nature from other organs, or as if, in adapting itself to obstacles affecting its action, it follows laws different from other muscular parts. The consequence of the neglect of this principle has been, that too often, in treatment of a valvular alteration in the heart, there has been a constant struggle between nature and medicine. Nature has been making the organ equal to its task; while medicine has been directed to counteract nature's efforts, and, by weakening the organ, to render it totally incapable of its task. The repeated bleedings, the starvings, the enforcement of debilitating measures, are totally unsuited to the disease we are considering.

Instead of such treatment, the measures most beneficial are those which, by strengthening the general constitution, will give a proportionate degree of vigour to the muscular power of the heart, and thus enable it to carry on the circulation in the absence of that assistance which it ought to receive. With this view,

a generous and sufficient diet of animal and vegetable food should be advised, at the same time that an abstinence from those beverages, such as malt liquors, which increase much the mass of the fluids, should be enjoined. It is not at all necessary that the patient should be prohibited from attending to his business or profession, provided that he do not devote to it so much attention as to produce debility. And as there is among patients who have learned that they are afflicted with heart disease an universal dread of sudden death, it is necessary to undeceive them on this point; and in the present instance it can be done with perfect safety, as the termination of the disease is never sudden. This plan of treatment, opposite to what has been generally enjoined, was forced upon the attention long before the reasoning adduced here had been brought to support it.

One case may be mentioned, out of many that occurred, showing the bad effects of debilitating treatment in the disease before us, and exemplifying the evil of acting as if one principle were sufficient for guiding us in the treatment of all heart diseases. It is now several years since a consultation was held upon the case alluded to. This treatment ordered was in accordance with that generally recommended, consisting of repeated small bleedings, blistering, the exhibition of digitalis, and the most rigid regulation of diet, a total abstinence from animal food, and even a spare allowance of vegetables and milk. At the time the patient, a young man, was put under this treatment, he was not in an alarming state; but the disease being recognized as heart disease, he had the fortitude to submit to a course which he was led to expect held out a prospect of cure. Bleeding after bleeding, and blister after blister, were repeated, starvation enforced, and digitalis exhibited, until the patient was reduced to such weakness that he had scarcely strength to raise himself in bed. The local disease was all this time, however, growing worse; for the palpitation, cough, &c. were, from the slightest cause, increased to greater violence than previously to the commencement of treatment. The plan was, nevertheless, persevered in, until the patient's death being supposed at hand, this debilitating treatment was discontinued. From that hour the patient got

better; and as muscular strength returned, the embarrassment of breathing, palpitation, cough, &c. became less and less urgent. The patient is still alive, the disease is still present; but, with full living and good air, he is able not only to take considerable exercise, but even to undergo the fatigue of a business that constantly requires very laborious exertion.

Having laid down the plan of treatment proper to be adopted as far as it produces effects upon the system, and through it upon the heart constituting a part of the system, it now remains to examine the propriety of employing in this disease a remedy such as *digitalis*, which produces a specific effect upon the heart rendering its action slow and weak, and which in consequence of that effect is usually recommended in cases of heart disease in conjunction with the measures already deprecated. In inadequacy of the aortic valves the pulse generally ranges from 90 to 110. After each contraction of the ventricle during the pause or interval of rest occurring between that contraction and the next following, a quantity of blood is regurgitating into the ventricle. The danger of the disease is in proportion to the quantity of blood that regurgitates, and the quantity that regurgitates will be large in proportion to the degree of inadequacy of the valves, and to the length of pause between the contractions of the ventricle during which the blood can be pouring back. If the action of the heart be rendered very slow, the pause after each contraction will be long, and consequently the regurgitation of blood must be considerable. Frequent action of the heart, on the contrary, makes the pause after each contraction short; and in proportion as the pauses are shortened, the regurgitation must be lessened. Instead, then, of regarding an increase of frequency in the action of the heart as an aggravation of the disease, it must be viewed, as we have already viewed hypertrophy of the heart, as a provision for remedying as far as possible the evil consequences arising from inadequate valves. To retard in such circumstances the action of the heart would be to do an injury. In every case of this disease in which *digitalis* has been administered, it has invariably aggravated the patient's sufferings. The oppression has become greater; the action of the heart



more laboured; the pulse intermittent, and very often dicrotic, from the heart's being unable by a single contraction to empty itself; general congestion and dropsy, if present, have been increased, and in some of the instances *bronchitis* from congestion has been induced; the respiration became laborious, and the strength so much sunk, that patients seemed almost moribund. From this state they only recovered by omitting the *digitalis*, and putting them on stimulants. In no case of this disease did *digitalis* produce the slightest good effect; and in all, the patients while under its exhibition were always worse.

A moderately quick pulse indeed is of itself no evil;—it is only an evil as an indication of some disease. In the present instance it is, however, an index of a positive good; it shows that the pauses between the contractions of the ventricle are short, and, consequently, that there is less danger of the quantity of blood thrown back upon the ventricle in the pause of its action, or intervals of rest, being of any considerable amount. The pulse, which in this disease ranges from 90 to 100, or even rises higher, is not to be interfered with merely because it is more frequent than natural. The more frequent action of the ventricle indicated by that pulse is a safeguard against regurgitation. In this respect permanent patency of the aortic opening differs from narrowing of the auriculo-ventricular opening. In permanent patency, as already explained, frequent contractions and short pauses are the best safeguard against regurgitation. In narrowing of the auriculo-ventricular opening, on the contrary, slow action of the heart is an object of the first importance; for a slow action of the auricle will allow more time for the passage of the blood through the narrowed opening, and thus diminish the regurgitation upon the pulmonary veins and the lungs.

Although depleting measures and a lowering plan of treatment have been deprecated in the management of inadequacy of the aortic valves, and although the continued employment of such measures in cases of this disease, instead of bringing relief, never fails to produce an aggravation of symptoms, there are, however, circumstances in which the most active treatment is called for. Inflammatory affections, congestions, &c. are more likely to occur

in patients suffering from any obstacle to the circulation than in others, and whenever these supervene in patients labouring under inadequacy of the aortic valves, whether they be inflammatory affections or congestions of the thoracic or abdominal viscera, they call for the most prompt and active treatment. Instead of the heart affection inducing us to be less active in our treatment, it is a motive to be more prompt than in ordinary cases. It may be a fatal mistake to suppose that the presence of the heart disease is to make our measures less energetic. Pneumonia, peritonitis, acute rheumatism, have occurred in some of the cases that have been under observation, and the patients have borne depletion even better than persons without any heart affection. It is a curious fact that, bleeding carried to a very large amount has never in these cases produced fainting. In this case the well-established principle, that in acute diseases the more prompt and decided the measures, the more rapid will be the recovery of the patient, and the less troublesome the sequelæ of the disease, should be our guide. The inflammatory affections that may incidentally occur in cases of inadequacy of the aortic valves, should be opposed with promptitude and decision; bleeding, when used, should be large; but when the inflammatory affection is once subdued, we should cease as soon as possible from debilitating treatment,—which, if persevered in, will prove injurious to the organic affection. No details need be given of the measures to be adopted in those incidental affections, because they differ in no respect, except in energy, from the usual treatment for the affection, whatever it may be, that has chanced to supervene. This active treatment on the occurrence of local inflammation is not at all incompatible with the course recommended to be followed when there is no disease present but the valvular inadequacy. Those incidental inflammatory or congestive affections will be rendered less likely to occur by the previous course of management recommended; for the greater vigour the system has enjoyed, the less danger there is of slight causes producing inflammation or congestion.

*Lastly*, There is besides the supervention of local inflammation or congestion, yet another circumstance, in which blood-letting

may be required. Without the occurrence of any apparently adequate cause, straitness of chest, difficulty of breathing tumultuous action of the heart, and a general feeling of nervous oppression are complained of. Neither pneumonia nor inflammatory action in any organ can be detected, and these symptoms seem to arise from an increase of bulk in the absolute mass of blood circulating, which keeps all the vessels so distended that the heart becomes oppressed, incapable of freely contracting, and tumultuous in its action. Relief is at once afforded by a large blood-letting, speedily followed by the exhibition of a full dose of an opiate. For the employment of the opiate, I am indebted to the suggestion of my colleague Dr. Hunt, and its good effects are such as to have no substitute for it. The employment of a large bleeding in either of the circumstances here detailed, is very different from the repetition of those irritating small bleedings that are usually practised.

Fits of coughing are sometimes very troublesome in the course of the disease, and where they arise from trifling bronchitis, they are best relieved by pectoral mixtures with a large proportion of opium, not less than four or five grains to an eight ounce mixture.

In these observations no medicine or treatment has been recommended with the view of acting directly on the aorta or valves, so as to restore in any degree the function of the latter. There is no medicine that can have any such power after the disease has been of much standing; and if the valves have become perforated or broken, it is obviously impossible to restore them to their original state. The disease is seldom seen in the commencement. Perhaps if seen early in those cases where it has followed an attack of rheumatism, or where it partakes of an inflammatory character, the employment of mercury pushed to salivation, and counter-irritation, might check the progress of the disease. In the advanced stages no good effect on the valvular affection has been produced by any or all of these measures.

Although the cure of *Inadequacy* of the Aortic Valves is probably out of the reach of medicine, a correct knowledge of the nature of the affection is not the less necessary. The patient is relieved from harrassing treatment, that, however applicable in

other cases of heart disease, is not alone useless, but positively injurious in this. In other affections of the heart there is a constant danger of sudden death from pulmonary apoplexy or hemorrhage, which may be induced even by ordinary exertion, and such danger keeps the patients in a state of perpetual terror. In this disease, on the contrary, assurance may be given against any sudden termination; and the patient may be permitted not only to attend to his business or profession, but may be assured, that, in leading a life of business and tolerable activity, he is adopting the very best means to prolong his life. Under treatment such as recommended, it is astonishing what little uneasiness inadequacy of the aortic valves will produce,—indeed, very often not so much as those organic affections or growth of the liver, which are nevertheless viewed by the profession and by patients with much less terror.

13, *Bachelor's Walk, Dublin.*



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THOMAS HODGKIN, M.D.  
Guy's Hospital Reports, 74, opp. 117, 1924

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## Thomas Hodgkin

English Physician, 1798-1866

### BIOGRAPHY

- 1798 Born August 17, at Pentonville, the third of four sons of John Hodgkin, a member of the Society of Friends and a grammarian. Learned Greek and Latin from his father.
- 1822 Age 24. Attended clinical instruction given at the Necker Hospital in Paris by the great Laennec.
- 1823 Age 25. Took the degree of Doctor of Medicine in the University of Edinburgh.
- 1825 Age 27. Became member of Royal College of Physicians of London. Appointed Curator of Museum of Guy's Hospital and Lecturer on Morbid Anatomy.
- 1832 Age 34. Described condition now known as Hodgkin's Disease.
- 1836 Age 38. Offered Fellowship of Royal College of Physicians of London but declined from conscientious motives.
- 1837 Age 39. Because of failure to receive post of assistant physician at Guy's Hospital, became attached to St. Thomas's Hospital.
- 1842 Age 44. Curator of the Museum and Lecturer on Practice of Physic at St. Thomas's Hospital.
- 1850 Age 52. Married a widow, Mrs. Sarah Frances Scaife.
- 1857 Age 59. Given 300 guineas as a testimonial but turned the money over to the Medical Benevolent College.
- 1866 Age 68. Died April 5, of dysentery at Jaffe, while traveling with Sir Moses Montefiore, who erected the monument over his grave.



Member of Senate of University of London.

Member of the Ethnological Society and for several years one of the vice-presidents.

Vice-President of the Geographical Society.

Founder of the Aborigines Protection Society.

Member of the British Medical Association.

Member of the Provincial Medical and Surgical Association.

Member of scientific societies in Rome, Sierra, Paris, Marseilles, Brussels, Ghent, Heidelberg, Philadelphia, Massachusetts, Catavia, Palermo and the Sandwich Islands.

Consulting Physician to the Dispensary for Diseases of the Skin.

Hodgkin, who always appeared in the Quaker dress, was a philanthropist and reformer by nature. He was not successful in private practice because of his carelessness in collecting fees and eccentric independence of spirit.

## EPONYMS

**DISEASE:** Called also infectious granuloma, malignant granuloma, malignant lymphoma, lymphomatosis granulomatosa, lymphadenoma and pseudoleukemia; a disease marked by an infectious granulomatous condition (inflammatory enlargement) involving particularly the lymphadenoid tissues of the body, beginning on one side of the neck and extending thence to the axillary, inguinal, mediastinal glands, and to the spleen. *On some morbid appearances of the absorbent glands and spleen.* Med.-Chir. Trans., Lond., 17: 68-114, 1832.

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## HODGKIN'S DISEASE

In 1832, while serving as curator of the Museum at Guy's Hospital, London, and lecturing on morbid anatomy, Thomas Hodgkin, being then 34 years of age, published a paper *On Some Morbid Appearances of the Absorbent Glands and Spleen*. He had published eight papers in the ten previous years, some of them relating to the physiology and pathology of the lymphatic system, so we know that his interest had been aroused for a considerable time toward a better understanding of this particular medical problem. Hodgkin was attempting to sort out a series of cases in which the lymphatic glands and spleen were the seat of disease. He was not endeavoring to describe a new condition and all of the seven patients he reported in detail did not have the same disease. Nevertheless, Hodgkin's name has clung to the type of case with painless progressive enlargement of lymph glands and spleen, leading to cachexia, anemia and finally death. His paper gives a short clinical picture of the patient, and rather complete post-mortem findings when possible, but concerns itself only slightly with a discussion of the true nature of the disease process. As he himself states in the opening paragraph, he was merely recording a series of findings which must have been observed by every morbid anatomist.

We retain the name Hodgkin's disease because of the publicity given this paper and condition by the devoted biographer of Guy's Hospital, Samuel Wilks, in 1865. He it was who, probably wishing to extend the glory of Guy's and The Great Men of Guy's, declared this disease to be a clinical entity and called it Hodgkin's disease.

When we realize that the original description was written before cells were even known, before cellular pathology and blood examinations, we must not wonder that Hodgkin knew so little but marvel that he knew so much.

At the present day, after tireless research by Longcope, Kofoed, Sternberg, Fraenkel and Much, Bunting and Yates and many others, Hodgkin's disease or, dropping the eponym, lymphadenoma is thought to be an infectious granuloma. It certainly is not a tuberculous process, although the two conditions may



coexist; the fact that no animals are susceptible has hindered progress. In 1902 a distinct contribution to our knowledge of the disease was made by Dorothy Reed who described (Johns Hopkins Hosp. Rep., 10: 133) a characteristic cell in the lymph nodes, the polynucleated giant-cell, now known as the Dorothy Reed cell. K. Ziegler, in a monograph in 1911, listed the following forms of the disease as now recognized: acute, localized, generalized, mediastinal, larval or latent, splenomegalic and osteoperiostitic. E. M. Medlar (Amer. Jour. Path., 7: 475, 1931) presented evidence which suggests that the disease is a malignancy of the bone marrow and the lymph node involvement merely metastatic. E. B. Krumbhaar (Amer. Jour. Med. Sc., 182: 764, 1931) suggested that the condition should be considered as a disease of the hemolytopoietic or the reticulo-endothelial system rather than of lymphoid tissue. In 1932, M. H. Gordon (Rose Research on Lymphadenoma, Bristol, John Wright and Sons, Ltd., 1932, p. 14, 48) observed a meningoencephalitic syndrome following the intracerebral inoculation of rabbits and guinea-pigs with a sterile suspension prepared from lymph nodes of typical Hodgkin's disease and in the ensuing year suggested this procedure as a valuable diagnostic aid. D. H. Rosenberg and L. Bloch advanced this work and reported their findings in Jour. Amer. Med. Assn., 106: 1156-1158, 1936.

We can only guess that if Hodgkin had dreamed of the discussion he was starting in 1832, he would have been compensated to a large extent for some of the unpleasantness of his life.

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# On Some Morbid Appearances of the Absorbent Glands and Spleen

BY

DR. HODGKIN

*Presented by Dr. R. Lee*

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**T**HE morbid alterations of structure which I am about to describe are probably familiar to many practical morbid anatomists, since they can scarcely have failed to have fallen under their observation in the course of cadaveric inspection. They have not, as far as I am aware, been made the subject of special attention, on which account I am induced to bring forward a few cases in which they have occurred to myself, trusting that I shall at least escape severe or general censure, even though a sentence or two should be produced from some existing work, couched in such concise but expressive language, as to render needless the longer details with which I shall trespass on the time of my hearers. (p. 69).

## *Case I*

November 2, 1826. Joseph Sinnott, a child of about nine years of age, in Lazarus's ward, under the care of J. Morgan. His brother, his constant companion with whom he had habitually slept, died of phthisis a few months previously; he was much reduced by an illness of about nine months, during which time he

had been subject to pain in the back, extending round to the abdomen. On his admission his belly was much distended with ascites. He had also effusion into the prepuce and scrotum. On the latter was a large ulcer induced by a puncture made to evacuate the fluid.

*Head.*—There was a considerable quantity of serous effusion under the arachnoid and within the ventricles. There were a few opaque spots in the arachnoid, but this membrane was in other respects healthy. The pia mater appeared remarkably thin and free from vessels. The substance of the brain was generally soft and flabby, but no local morbid change was observable.

*Chest.*—The pleura on the right side had contracted many strong and old adhesions, in addition to which there were extensive marks of recent pleuritis. On the left the pleura was nearly or quite free from adhesion, but there was some fluid effused into (p. 70) the cavity. There was some little trace of a tubercular cicatrix at the summit of the right lung, but the substance of both lungs was generally light and crepitant, with a very few exceedingly small tubercles scattered through them.

The mucous membrane exhibited an excess of vascularity; the bronchial glands were greatly enlarged and much indurated.

The heart appeared quite healthy.

*Abdomen.*—There was extensive recent inflammation of the peritoneum, in the cavity of which there was a copious sero-purulent effusion, and the viscera were universally overlaid with a very soft light yellow coagulum, too feeble to effect their union, though evidently having a tendency to do so. The mucous membrane of the stomach and intestines was generally pale and of its ordinary appearance, but in some few spots it was softened and readily separated itself from the subjacent coat. The contents of the intestines were copious and of an unhealthy character, overcharged with bile. The mesenteric glands were generally enlarged, but one or two very considerably so, equalling in size a pigeon's egg, of semi-cartilaginous hardness and streaked with black matter. The substance of the liver was generally natural, but contained a few tubercles somewhat larger than peas, white, semi-cartilaginous, and of an uneven surface. The (p. 71) pancreas

was firmer than usual, more particularly at its head, which was somewhat enlarged. The spleen was large and contained numerous tubercles. The absorbent glands about both the two last-mentioned organs were much enlarged. Both kidneys were mottled with a light colour, but were free from induration. A continuous chain of much enlarged indurated absorbent glands of a light colour accompanied the aorta throughout its course, closely adherent to the bodies of the vertebræ, and extended along the sides of the iliac vessels as far as they could be traced in the pelvis. None of these vessels had been sufficiently compressed to occasion the coagulation of the contained fluids. The coats of the thoracic duct, which was large, were perfectly transparent and healthy.

### *Case II*

September 24, 1828. Ellenborough King, aged ten years, was admitted into Luke's ward on the 6th of August, 1828, under the care of Dr. Bright. He was the youngest of six children, of whom the first five were reported to be all healthy. This child had also been healthy till about thirteen months ago, when his strength, flesh, and healthy appearance began to fail. He was at that time living in the west of England. A tumour was observed in the left hypochondrium in the situation of the spleen, the glandulæ concatenatæ on the right side were observed to be considerably enlarged, but under the treatment employed, (p. 72) these tumours, as well as that in the situation of the spleen, were at times very considerably reduced in size.

It does not appear that he was ever subject to hæmorrhage, nor till very lately to dropsical effusion; his appetite was generally good. After his admission into the hospital the tumour on the left side was observed to extend considerably below the left hypochondrium, but was reported not to be so large as it had formerly been. The glands on the left side of the neck were swollen, as well as those on the right, the abdomen was somewhat distended, and there was considerable œdema of the scrotum.

The head was not opened.

The glands in the neck had assumed the form of large smooth ovoid masses, connected together merely by loose cellular mem-

brane and minute vessels: when cut into they exhibited a firm cartilaginous structure of a light colour and very feeble vascularity, but with no appearance of softening or suppuration. Glands similarly affected accompanied the vessels into the chest, where the bronchial and mediastinal glands were in the same state and greatly enlarged. There were some old pleuritic adhesions. The substance of the lungs was generally healthy. There was a good deal of clear serum in the pericardium, but this membrane, as well as the heart, was quite healthy.

In the peritoneal cavity there was a considerable (p. 73) quantity of clear straw-coloured serum mixed with extensive, recent thin diaphanous films. The mucous membrane of the stomach and intestines was tolerably healthy.

The mesenteric glands were but slightly enlarged, and but little if at all indurated; but those accompanying the aorta, the splenic artery, and the iliacs were in the same state as the glands of the neck.

The liver contained no tubercles, and its structure was quite healthy. The pancreas was rather firm, and the glands situated along its upper edge, were, as before stated, greatly enlarged. The spleen was enlarged to at least four times its natural size, its surface was mammillated, and its structure thickly sprinkled with tubercles, presenting the same structure as the enlarged glands already described.

### *Case III*

By H. Peacock, Esq.

November 28, 1829. William Burrows, aged about thirty years. He was admitted into Naaman's ward on the 26th of September, 1829, under Mr. J. Morgan, for ulcers of a scrofulous character in the axilla and neck, accompanied with general cachexia; he had previously been a patient in Samaritan's ward with secondary symptoms of syphilis, (p. 74) and was supposed to have taken large quantities of mercury.

About four months before his death, which occurred on the 27th of November, abdominal dropsy made its appearance.

The body was extremely emaciated, some ragged excavated ulcers were situated about the right axilla and thorax; the ulceration extended beneath the neighbouring skin, and between the pectoral muscles. The muscles of the body were pale.

The head was not examined.

The left cavity of the chest contained about a pint of serum. The lung was rather œdematous, but otherwise healthy, with the exception of some puckering and apparently chalky deposit at its apex. The lung on the right side adhered closely to the walls of the cavity, the adhesions being firm and cellular. The lung resembled that of the left side, and was also slightly disorganized at its apex. The pericardium contained about an ounce of clear and straw-coloured fluid. The heart was small and flabby.

The abdomen contained about two pints of clear serum. The stomach and alimentary canal were much distended with flatus. The liver was of a shrunk irregular shape, and was connected to the (p. 75) diaphragm by a few firm adhesions. Its structure was indurated, pale, and thickly pervaded with a substance having a white, hard, tuberculous character which in some parts had the form of defined rounded masses of the size of large pin heads, but for the most part was diffused. Some sections exhibited parts apparently stained with a dark ecchymosis as if from extravasated blood.

From some portions of liver seen after the inspection by Dr. Hodgkin, it appeared to him that the liver was in that state in which the acini became dense, rounded, and of a light colour, resembling small tubercles, and are readily detached: a condition of liver which is almost peculiar to those who have laboured under a cachectic condition from mercury. The gall-bladder was small and filled with a dark coloured green bile. The pancreas was not diseased. The spleen had contracted several firm adhesions to the neighbouring peritoneum; it was enlarged to about twice its usual size, and was unusually firm. Sections exhibited its structure dense, rather dry, and of a dark red colour, but homogeneous. Dr. Hodgkin examined this spleen, a short time after its removal from the body, and found its substance generally pervaded by numerous minute translucent bodies somewhat

resembling incipient miliary tubercles of the lung, but considerably smaller than these generally are.

The kidneys were pale, flabby, and slightly mottled.

(p. 76) A few small miliary tubercles were found in the peritoneum, about the inguinal region resembling those which have been noticed above in the liver. Some of the mesenteric glands were much enlarged and filled with a firm white deposit. The inguinal, lumbar, and aortic glands were similarly affected. The bronchial glands were in a similar state, and also extensively ossified (or loaded with earthy matter). The axillary glands were in a state of suppuration, and exposed by ulceration at the part. The thoracic duct presented nothing unusual.

#### *Case IV*

January 8, 1830. Thomas Westcott, aged apparently about fifty years, by trade a carpenter, a patient of Dr. Addison in the Clinical Ward, admitted 30th of December, 1829. He was not at all wasted, but was rather plump than otherwise; he had a pale and peculiar, cachectic countenance, which, without minute description, may be suggested to the mind by comparing it to what is seen in some cases of confirmed disease of the spleen. The most remarkable feature in his case was the great enlargement of nearly, if not quite, all of the absorbent glands within reach of examination, but more especially in the axillæ and groins. Those at the side of the neck were scarcely less so. Most of these glands which were within reach, were of about the size of pigeon's eggs, a few somewhat larger, and others rather smaller. They were of a smooth (p. 77) rounded or ovoid figure, and were only moderately firm, rather than indurated. An enlargement was also to be felt in one epididymis. The abdomen was distended, but the substance of the parietes appeared thick, no distinct tumour could be felt in the region of the spleen, or in any other part of the abdomen.

The functions of the brain had been somewhat disturbed, and the left eye did not see so well as the right.

It did not appear that this patient had been liable to any particular exposure, nor could any circumstance be referred to as the

exciting cause of his malady. His death took place very suddenly in the morning of the 8th, and the examination was made four hours and a half after.

The veins of the head and neck were turgid. There was no lividity of the face. There were some ecchymosed spots on one of the legs.

The arachnoid was remarkably thick and opaque. On the surface of the right hemisphere there was a diffused light rose-red colour, occupying the space of about the size of a crown piece; it appeared to depend on infiltration of the pia mater. This membrane separated readily from the surface of the brain. No morbid appearance was discovered in the substance of the brain, and no undue quantity of fluid (p. 78) in the ventricles. The cerebellum seemed to be, proportionately, rather small.

The right optic nerve was rather smaller than its fellow.

The glands in the axillæ and neck, as might have been expected, were found prodigiously enlarged, the deepest seated being in general the largest. The cellular structure around these was loose and free from any morbid deposit. These glands were smooth and of a whitish colour externally, with a few small bloody spots. When cut into, their internal structure was likewise seen to be of a light, nearly white, colour with a few small interspersed vessels. They were of a soft consistence, which might be compared to that of a testicle. They possessed a slight translucence, and were nearly or quite uniform throughout, exhibiting no trace of partial softening or suppuration. Although in appearance and consistence these enlarged glands bore considerable resemblance to some fungoid tumours, they presented nothing of the encysted formation. The alteration in this case seemed to consist in an interstitial deposit from a morbid hypertrophy of the glandular structure itself, rather than on a new or adventitious growth. The glands in the groin presented precisely the same character as those just described; the same may also be said of those in the thorax and abdomen, the situation and extent of which will be presently stated.

(p. 79) The pleuræ were nearly, if not altogether, free from adhesions and effusion. There were a few ecchymosed spots on



the posterior part of the right lung; both lungs were spongy and crepitant, but rather emphysematous, and of a light colour, from the small quantity of blood which they contained.

The bronchial tubes contained some thick mucus.

The pericardium was healthy. The heart was greatly enlarged, and the right cavities particularly dilated; but the left were also large and distended, with thickened parietes. The muscular structure however did not appear to be diseased. The blood in the heart was barely coagulated, resembling that recently drawn into a basin. The glands along the subclavian arteries and about the roots of the bronchi were much enlarged.

In the abdomen nothing particular was noticed about the peritoneum. The glands at the small curvature of the stomach, several in Glisson's capsule, and a large mass of them along the entire course of the abdominal aorta and iliac arteries were greatly enlarged. There was a marked difference in the mesenteric glands, which, though larger than is natural, were none of them of the prodigious size of those above mentioned; they were however of a light colour, and their increase of size evidently depended on an interstitial deposit similar to that of the other glands. One of the enlarged glands (p. 80) in the lumbar region had a good deal of superficial ecchymosis. The absorbent vessels connected with it were enlarged and distended with a bloody serum. A similar fluid less deeply tinged was found in the thoracic duct.

The liver was very large, pale, and slightly granular. The spleen was very greatly enlarged, being at least nine inches long, five broad, and proportionally thick; its colour was lighter and redder than is natural, and more firm and close. On cutting into it an almost infinite number of small white nearly opaque spots were seen pervading its substance; they were of irregular figure, but a few appeared nearly circular. They appeared to depend on a deposit in the cellular structure of the organ. There were no tubercles in the spleen, but the spots just mentioned were perhaps a commencement of this kind of formation.

The pancreas was large and pale, but otherwise healthy. The mucous membrane of the stomach and bowels offered nothing remarkable.

*Case V*

Inspection of a middle aged man, who had latterly been a patient of Dr. Back. He had long been in bad health, and had been for some time a patient under Dr. Bright. His last most urgent symptoms were referrible to the chest. When in the hospital (p. 81) the former time, he was observed to have the glands of the neck, and more particularly those near the upper part of the thyroid cartilage, considerably enlarged.

The body was emaciated. The glands before mentioned were still much enlarged, those in the axillæ were not observed to be particularly so, those in the groins were somewhat so. The abdomen was distended.

The head was not examined.

The greater part of one lung was distended, solid and void of air, its texture was rather soft and readily lacerable. Its colour seemed to be the result of the acute white hepatization very deeply soiled with reddish brown. The other lung was far from healthy, but it was rather engorged and softened than hepatized, and still contained air. One, if not both, pleuræ exhibited traces of recent inflammation with little or no effusion.

Nothing remarkable is remembered to have been noticed in the heart or pericardium.

In the abdomen there was a large quantity of serum with little appearance of coagulable lymph. In the stomach the mucous membrane was not quite healthy, presenting some indications of chronic inflammation; it, as well as the intestines, contained (p. 82) unhealthy secretions. The liver was of remarkably large size, weighing upwards of seven pounds. Its form and the smoothness of its surface were little if at all altered. The colour was somewhat mottled with a mixture of darkish green and yellow. The acini were manifestly enlarged, and it was suspected that they had undergone the fatty degeneration; but on exposure to heat, it appeared to contain little, if any, greasy substance. The spleen was very large, its weight is not known, but it appeared to be four or five times the average size; its texture was rather more solid and compact than is natural; it contained no tubercles, but the cellular structure interspersed through the parenchyma was

more conspicuous than is usual, in some parts appearing in the form of specks, in which it was soft and easily broken down. The absorbent glands accompanying the aorta were greatly enlarged, some equalling at least the size of a pullet's egg; some, but more especially those in the abdomen, were reddened by injected or ecchymosed blood. The receptaculum chyli and some of the larger lymphatic branches, contained blood mixed with dark and almost black coagula. The thoracic duct, which was large, was filled in the same manner.

### *Case VI*

July 19, 1830. Thomas Black, aged about fifty years, admitted into Barnabas Ward on the 30th of June, 1830, under the care of Dr. Bright. He was affected with large tuberosc swellings of considerable (p. 83) firmness on both sides of the neck, in both axillæ, and in both groins. His abdomen was greatly distended, he suffered from difficulty of breathing, and was pale and rather emaciated.

It appeared that, about two years before, he had laboured under fever. That, being exposed to cold, shortly after, he observed the glands swell on one side of the neck; not long after on the other side, and in succession, those in the situations above mentioned.

The body presented considerable lividity, especially the extremities on the left side. The left side of the neck, and the left axilla, presented the largest tumours.

The head was not examined.

The tumours evidently depended on greatly enlarged absorbent glands along the course of the carotic and axillary arteries. On raising the sternum they were found to extend along the subclavians and internal mammaries; they were also found, though in less number and size, along the aorta in the posterior mediastinum; but it did not appear that the bronchial glands were at all similarly affected. There was some appearance of recent pleuritis and serous effusion into the chest.

In the peritoneal cavity there was a large quantity (p. 84) of yellow serum mixed with some flakes of lymph. A large and

continued mass of nodulous glandular tumours surrounded the aorta and iliac arteries, but the mesenteric glands were very slightly affected. The omentum was corrugated. The liver was rather small, with an irregular and uneven surface, its colour was lighter than natural, and the acini were converted into rounded fleshy masses, without any very great change in the intervening cellular membrane. It also contained two or three white tubercles, which resembled fungoid tubercles of the liver, and were situated at the surface of the organ. The structure dependent on cysts was not demonstrable in them, but from their form it might be suspected. The spleen was of moderate size, and appeared to be quite free from any adventitious deposit, which is a fact worthy of remark, as in very many cases of glandular disease bearing resemblance to the present case, this organ has been affected, and generally tubercular. The pancreas was imbedded in the tumours, but appeared pretty healthy.

The kidneys were livid and congested.

The tumours which formed the most striking features in this case very nearly resembled each other in structure; there appeared to be merely a little difference in firmness; they were of various sizes, from that of a horse-bean to that of a hen's egg; they had a round or ovoid figure, and were invested by a thin membrane, pretty smooth externally, and (p. 85) connected to the loose and apparently healthy cellular membrane which surrounded the tumours; the other surface intimately adhered to the structure of the tumour. This texture was apparently pretty uniform throughout, and was pale and slightly translucent, and could not be said to evince traces of the mode of formation dependent on cysts; they shewed no disposition to suppuration or softening; some, when just taken from the body, were of a semi-cartilaginous hardness, but became considerably softer after a little maceration.

The aorta appeared to be a little compressed by the tumours.

This patient had an old reducible hernia on the right side, on which side there appeared to be hydrocele also.

It may be observed that notwithstanding some differences in structure, to be noticed hereafter, all these cases agree in the remarkable enlargement of the absorbent glands accompanying

the larger arteries; namely, the *glandulæ concatenatæ* in the neck, the axillary and inguinal glands, and those accompanying the aorta in the thorax and abdomen. That as far as could be ascertained from observation, or from what could be collected from the history of the cases, this enlargement of the glands appeared to be a primitive affection of those bodies, rather than the result of an irritation propagated to them from (p. 86) some ulcerated surface or other inflamed texture through the medium of their inferent vessels, and that although, in some instances, the glands so enlarged may contain a little concrete inorganizable matter, such as is known to result from what is called scrofulous inflammation, it is obvious that this circumstance is not an essential character, but rather an accidental concomitant to the idiopathic interstitial enlargement of the absorbent glandular structure throughout the body. That unless the word inflammation be allowed to have a more indefinite and loose meaning than is generally assigned to it, this affection of the glands can scarcely be attributed to that cause, since they are unattended with pain, heat, and other ordinary symptoms of inflammation, and are not necessarily accompanied by any alteration in the cellular or other surrounding structures, and do not shew any disposition to go on to the production of pus or any other acknowledged product of inflammation except where, as in the cases above alluded to, inflammation may have supervened as an accidental affection of the hypertrophied structure. Nor can the enlargement in question, with any better reason, be attributed to the formation of any of those adventitious structures, the production of which I have already had occasion to describe, and have referred to the type of compound adventitious serous cysts. Notwithstanding the different characters which this enlargement may present, it appears nearly in all cases to consist of a pretty uniform texture throughout, and this rather to be the consequence of a general increase of every (p. 87) part of the gland, than of a new structure developed within it, and pushing the original structure aside, as when ordinary tuberculous matter is deposited in these bodies. At the same time it must be admitted that the new material by which the enlargement is effected, presents various degrees of

organizability, which in some instances is extremely slight, and appears incompetent to maintain the vitality of the affected gland. In such cases the new structure will generally become opaque, soften, or break down, and acting as a foreign irritating body, excite irritation and lead to the formation of abscess. The case of William Burrows, (No. III.,) and also that of a native of Owhyhee, who died in Guy's Hospital with extensive abscess in the axilla, are, I believe, to be considered of this kind.

The remarkable appearance of blood in the thoracic duct and some of the absorbents, observed in the case of Thomas Westcott, (No. IV.,) although it sufficiently attracted my attention to induce me to have a drawing immediately made, was only regarded as an accidental occurrence; but the recurrence of the same phenomenon to a much more considerable and striking extent in the recent case, (No. V.,) induces me to suppose that it is intimately connected with this glandular disease. It may also be observed that in the last-mentioned case the enlarged glands from which the lymphatic vessels containing blood proceeded, were particularly loaded with blood; and if my recollection does not deceive me, a tendency to (p. 88) the same state was present in the case of Westcott, although it escaped notice in the record of the inspection.

Another circumstance which has arrested my attention, in conjunction with this affection of the absorbent glands, is the state of the spleen which, with one exception in all the cases that I have had the opportunity of examining, has been found more or less diseased, and in some thickly pervaded with defined bodies of various sizes, in structure resembling that of the diseased glands. We might, from this circumstance, be induced to suspect that these bodies in the spleen, like the enlarged glands themselves, are the result of the morbid enlargement of a pre-existing structure, an idea which may derive some support from the fact, that although in human spleens no glandular structure is distinguishable, in those of some inferior animals a multitude of minute bodies exist which appear to be of that nature. Malpighi indeed considered the acini or granulations in the spleen to be glands. In one instance it may be remarked that although the glandular

derangement had advanced very far, the depositions in the spleen were extremely minute, assuming the appearance of miliary tubercles. Hence, we may conclude that if, as I conceive to be the case, there be a close connection between the derangement of the glands and that of the spleen, the latter is a posterior effect, and on this account may not always have been produced, when that of the glands or some other disease (p. 89) carried off the patient. In other instances, the spleen, although much enlarged, contained no regular defined bodies, although the white cellular structure was very evident in increased quantity pervading the dense and enlarged mass of the organ. In such cases it might still be doubted whether, had the patient's life been protracted, the deposits in question might not ultimately have taken place, yet I am inclined to believe the contrary, and to suspect that either the previous derangement of the structure of the organ or the greater age of the patients may have opposed their production. I mention this effect of age merely as a suspicion or idea, founded on the fact that I have very rarely, if ever, met with any kind of tubercles, excepting those of malignant character, in the spleens of adults, whilst they have been by no means unfrequent in a far less number of spleens of children and young persons which it has fallen to my lot to examine. The only exceptions which I can call to mind, as having been furnished by my own observation, have been in the case of one or two foreigners from warm countries, on whom the change of climate may have had considerable effect.

Some further confirmation of my suspicion that a connection exists between the glandular derangement of which I have been speaking, and the state of the spleen, has occurred to me since the preceding observations were written. Whilst examining the unrivalled collection of pathological drawings made by my friend Dr. Carswell, I was struck with one representing (p. 90) a greatly enlarged spleen, loaded with large tubercles of a rounded figure and light colour. I immediately recognized it as a fine example of the affection I have been describing, and my suspicions were presently confirmed by the doctor's shewing me another fine drawing of the greatly enlarged glands of the neck, axillæ, and groins of the same subject.

The Doctor has favoured me with a copy of the case, and allowed me to place the drawings themselves before you.

## *Case VII. "Cancer Cerebriformis of the Lymphatic Glands, and of the Spleen"*

"The delineations of this very remarkable case were taken from a man who died in the hospital St. Louis at Paris, in the month of April. Monsr. Lugol, one of the physicians of the hospital, and under whose care the patient was, has promised to give me the particulars of this case. I was told, however, that the patient, who was between thirty and forty years of age, stout made, and not lean, had been affected with swelling of the glands under the jaws, along both sides of the neck, in the axillæ and groins for between three and four months, from which he had suffered but little inconvenience, to which he had paid but little attention, and had employed no remedies. It was only a short time before he applied to be taken into the hospital that he felt a (p. 91) difficulty in swallowing, which rapidly increased, and for the last two or three days was such as to prevent him from taking any kind of food whatever. As his appetite had never been affected by the disease, he was, when he came to the St. Louis hospital, in a state of great suffering, not only from want of food and from debility, but from the idea that he was rendered incapable of satisfying the cravings of hunger, together with the prospect of inevitable death.

"He lived rather more than two days.

"*Inspection of the body.*—On each side of the neck were large groups of glands extending from the angle of the jaw down to the clavicle, where they were joined to another group, coming up from the axillæ and passing under the clavicle. The submaxillary and sublingual glands were greatly enlarged, and united with the other lymphatic glands, formed an almost continuous chain stretching along the border of the jaw, and uniting under the chin. These glands were of various sizes, some of them were not larger than a pea, while others were as large as a hen's egg; they were round, oval, or of an irregular form, particularly where they were united by a common capsule. A great many of them presented the colour which distinguishes them in the healthy state; others



were of a yellowish tinge, with more or less redness and vascularity; whilst a few were of a deep red colour and highly vascular. The (p. 92) greater number of them when pressed between the fingers, felt pretty firm and somewhat elastic; those that were red and vascular were softer. All of them were enclosed in a thin but firm capsule, which contained a substance of the colour and consistence of brain, and in which were distributed a considerable number of blood-vessels. In the softest the vascularity was such as to give to the cerebriiform matter an appearance resembling a mixture of equal parts of brain and blood. A similar state of the glands was observed in both groins. The greater number of them were as large as pigeons' eggs, and could be followed passing upwards under Poupart's ligament, surrounding the great blood-vessels, and terminating in the diseased lymphatic and mesenteric glands. The diseased appearances observed in the glands of the groin are represented in No. 4—6. Fig. I; those of the neck and axillæ No. 4. a. In No. 4—6 is seen the appearance of the substance of which the glands were formed; in one of them the vascularity of this substance is seen to be very great, whilst in the other the vessels are few in number, long, and slender. The quantity of cerebriiform matter is also seen to differ considerably in each. Besides, in the lower figure the lobulated structure which it presents is pretty well marked. In Fig. III. two of the glands are represented after having been injected. In the upper one a large vein is seen coming out from it, and arising from a great number of minute vessels, which apparently are situated near the surface of the gland. In the lower one, the corresponding artery is shewn, (p. 93) dividing and subdividing into an immense number of extremely fine branches which are distributed throughout the substance of the gland. No. 4. c. Fig. I. represents an enormous tumour formed by the lymphatic glands situated under the liver, duodenum, pancreas, and great blood-vessels of these parts. It was as large as an adult's head, projecting forwards on a level with the convex surface of the liver, and carried before it the duodenum, pancreas, and gall-ducts, which passed over its anterior surface. Fig. II. represents a section of this tumour, which is seen to be formed of a great number of glands, some of which are as large as a small orange. Like those

of the neck and axillæ, they were composed of cerebriform matter, possessing a greater or less degree of vascularity. In the centre of the tumour considerable hemorrhage had taken place, the centre of the hemorrhagic effusion was occupied by coagulated blood, and the circumference by layers of fibrine. The vena cava and aorta passed through the tumour, and the former was nearly perforated by one of the diseased glands.

"No. 4. c. Represents the same pathological condition in the glands situated in the posterior fauces. The glands situated around the root of the tongue were so much enlarged as to shut up completely by their projecting upwards, backwards, and forwards, the posterior nares and superior aperture of the œsophagus. I could not ascertain the precise state of the epiglottis, but it must to a certain (p. 94) extent at least have been free, as it did not appear that inspiration had been much impeded. The amygdalæ, formed entirely of cerebriform matter, presented a pale-yellow colour tinged here and there with red specks, produced apparently from the rupture of minute blood-vessels. They have also lost that characteristic appearance from which they derive their name, having become almost perfectly smooth from the accumulation of the cerebriform matter and the distention of their envelope.

"The spleen was the only organ apart from the lymphatic glands which represented a similar, or indeed any, disease in this remarkable case. The external surface of this organ is shewn in No. 4. a. Fig. I. Besides great increase of its bulk, it presented externally a great number of irregular elevations surrounded by redness and vascularity. When divided longitudinally, Fig. II., it appeared to be formed entirely of cerebriform matter and fine blood-vessels; hardly any trace of its natural structure being observable. It presented a lobulated structure; the lobules varying from the size of a small pea to that of a large gooseberry; these being again divided and subdivided into smaller ones—the boundaries of the lobules and the intersections of the latter were the parts in which vascularity was greatest—it did indeed appear as if the lobulated structure had been the result of a vascular network so disposed as to inclose and separate more or less completely portions of different sizes of the cerebriform matter. It (p. 95)

depended, however, in all likelihood, on the structure of the spleen, in the cells of which, or in the blood which they contain, the cerebriiform matter was deposited or formed, whilst the blood-vessels which surrounded the lobules and ramified in their inter-sections arose from those which belong to the splenic cells.

"The body having been removed by inadvertence before I had time to examine the chest, I did not ascertain the state of the bronchial glands, but I was informed by one of the house-physicians that they were not diseased."

Although the Doctor has employed the term "cerebriiform matter," which conveys a ready idea of the texture of the diseased glands, he will excuse my differing from him so far as to regard the affection in this case as distinct from cerebriiform cancer. I feel the less difficulty in doing so, in the recollection that one of the cases of which I had given the details was, like Dr. Carswell's, considered as fungoid until a special and close inspection had detected the difference.

Besides the preceding cases, of which I have been enabled to obtain the inspections, I have met with other examples in the living subject which, as far as the glands were concerned, were evidently of the same character with those I have been describing. One of the most remarkable occurred in the person of a Jew, apparently between forty and fifty years of (p. 96) age; the glands in the neck were prodigiously enlarged, forming smooth ovoid masses, unaccompanied by inflammatory symptoms or thickening of the surrounding cellular structure. The glands in the axillæ and groins were in the same state; in fact, in this case, the enlargement was more considerable than in any other that I have witnessed. His general health was much impaired; I do not recollect that there were any dropsical symptoms at the time I saw him. I accidentally lost sight of him, but afterwards learnt that he died about two months from the time of my seeing him.

Another case occurred in a cachectic, rather emaciated child, who was brought, on one occasion only, as an out-patient, to Guy's Hospital. The glands in the neck, axillæ, and groins were considerably enlarged, and as far as I could judge were of the firm character observed in the cases of Joseph Sinnott and Ellen-

borough King, rather than the softer and more fleshy character noticed in the glands of Westcott, Black, Case V, and as far as I could observe, in that of the Jew just mentioned.

A pathological paper may perhaps be thought of little value if unaccompanied by suggestions designed to assist in the treatment, either curative or palliative; on this head however I must confess that I have nothing to offer.

Most of the cases, it may be observed, were those (p. 97) of patients in the hospital, where they had not sought admission until the disease had reached an advanced and hopeless stage. The Jew was the only individual whom I had an opportunity of treating myself, and him only for a short period, when his case had already become hopeless. The cascarrilla and soda which were given with a view to improve his general health, and the iodine employed as the agent most likely to affect the glands, appeared to be productive of no advantage, on which account it is probable the patient withdrew himself from my observation. Were patients thus affected to come under my care in an earlier and less hopeless period of their malady, I think I should be inclined to endeavour as far as possible to increase the general vigour of the system, to enjoin, as far as consistent with this object, the utmost protection from the inclemencies and vicissitudes of the weather, to employ iodine externally, and to push the internal use of caustic potash as far as circumstances might render allowable. I mention this last part of the treatment in consequence of the strong commendation which Brandrish has bestowed on the use of this caustic alkali in absorbent glandular affections. The views which I have been induced to take respecting the functions of the absorbent vessels, would make me the more disposed to adopt it\*.

\* Shortly after the reading of this paper, I was favoured with the following communication from my friend G. O. Heming, of Kentish Town:—  
Dear Sir,

You will, I am sure, be pleased with the following extract from Malpighi.

Yours truly, G. O. HEMING.

"In homine difficiliter emergunt (speaking of the granules in the spleen): si tamen ex morbo universum glandularum genus turgent, manifestiores redduntur, auctâ ipsarum magnitudine, ut in defunctâ puellâ observavi, in quâ lien globulis conspicuis racematim dispersis totus scatebat."

(p. 98) Having been led to notice some morbid appearances in the spleen connected with the glandular disease of which I have been speaking, I take the opportunity, before quitting this organ, to advert to another morbid appearance presented by it. In the observations prefixed to the sixth section of the second part of the catalogue of Guy's Museum\*, I have briefly noticed a derangement of structure met with in the spleen, which arrested my attention, rather from considering (p. 99) it as hitherto undescribed, than from having reason to attach any importance to it in conjunction with disease. The cases which I have since met with have not only thrown further light on its nature, but have shown that it may become the cause of violent and even fatal symptoms. The partial induration of the spleen accompanied with loss of colour, and in general with a diminution of bulk, and having at first sight a good deal of the appearance of tubercle, seems to be only one of the stages in which this derangement of the spleen presents itself to our view. It appears to commence in a partial extravasation of blood, the character of which will perhaps be best conceived by stating it to be what would be called by some pathologists apoplexy of the spleen. This I had already conceived to be the case, and suspected that it arose from external violence. The case of Mary Hamblin, No. I., tends to confirm this suspicion: it is however by no means improbable that spontaneous or idiopathic apoplexies of the spleen may take place. Yet the general appearance of the lesion will, I believe, form a characteristic distinction between such cases and those in which external violence had been the cause.

\* "The preparations from 2000 to 2004 inclusive, although of but little pathological importance, possess some interest as specimens of a morbid appearance occasionally met with in the spleen, but which, so far as the author knows, has not been hitherto described or noticed. It consists of a partial or circumscribed degeneration of the structure which becomes preternaturally firm and dense, and of a light colour. The part thus affected may be easily mistaken for a tubercle, until close inspection has detected in it traces of the original structure of the organ. It is bounded by a defined line, and on the surface there is sometimes a slight depression where it is united to the healthy structure. In all the instances which the author has yet observed, the portion of spleen thus degenerated has been situated in a transverse direction. He has observed it principally, if not exclusively, in males, and he is inclined to consider it as the result of external injury."—Vid. Catalogue of the Museum of Guy's Hospital. Part II. Sect. 6.

When the effusion of blood is quite recent, the part affected is distinguished from the other parts of the organ, not only by its increased density, but by its deep venous hue. It does not remain long in this state, but soon begins to assume a brownish colour, (p. 100) the change generally taking place at the circumference, but sometimes at the centre. This change, the rationale of which is not easily given, is precisely similar to that which takes place in apoplexy of the lungs, in the transition of the red into one of the grey forms of induration of the lung from inflammation; in the coagula sometimes met with in the heart and vessels; in the layers of aneurismal tumours; and even in cerebral apoplexy.

The portion of spleen thus altered, although possessing little perceptible trace of organization, may yet retain its vitality, and remain a permanent structure, in which case its density increases, but its bulk contracts, and a thin semi-transparent boundary may be seen to separate the altered from the healthy structure of the organ; this I conceive to be occasioned by the former not participating in the constant variations of dimension to which the latter is liable. It was in this state that the derangement of which I am speaking first presented itself to my attention. (See 2d, 3d, and 4th Examples.)

Although, as I have remarked, the derangement in question, when arrived at this stage, may remain quiescent for an indefinite length of time, and perhaps never throughout the life of the individual give rise to the slightest inconvenience; yet, it would seem to predispose the adjoining parts of the organ to derangement either from external force, or from unusual (p. 101) distension. In the 5th Example, this disturbance appears to be extremely slight, only amounting to a slight appearance of extravasation or apoplexy.

In the sixth case, that of Maria Lowther, the derangement in the structure of the spleen, in the neighbourhood of the indurated portion, was much more considerable, amounting to complete softening, accompanied by softening in the central part of the degenerated spot. It appeared pretty evident that this state of the spleen was the exciting cause of the severe peritonitis, in the same way that this inflammation is not unfrequently set up by

disease in the appendix cæci from feculent concretions. It is also highly probable that some of the remarkable symptoms which attended this case, and excited the idea of phlebitis, were also dependent on what may be considered as the gangrenous softening of the substance of the spleen in contact with the indurated part. No light was thrown on the cause which excited this softening, but if my suspicions are correct as to external injury being the cause of the original derangement, it is likely that a repetition of this cause, may promote the secondary affection by producing a slight laceration on the surface of the indurated part. Although the sudden death of the patient who formed the subject of the seventh case was rather to be attributed to the heart than to the state of the spleen, yet I think we must principally ascribe to this latter cause, the symptoms under which this girl had laboured, and more especially (p. 102) those paroxysms which were regarded as occasioned by intermittent fever.

My enquiries in this case also did not succeed in leading to any information as to the mode in which the process of softening had been excited. It is possible that slight external violence may have been adequate to this effect. It may, however, be queried whether intermittent fever had not actually existed, in the cold stage of which the spleen being gorged may have sustained a partial laceration where its distension was restrained by the unyielding character of the previously degenerated portion. Be this as it may, there can be but little doubt that the occurrence of such paroxysms would either occasion such a disorganization, or greatly aggravate it when once set up.

#### *No. I*

May 3, 1831. Mary Hamblin, a patient of Dr. Bright's, in Charity Ward, admitted April 27th, 1831, in consequence of a state of mania, in which she was reported to have been a little more than a week. She was the mother of twins, whom she had suckled sixteen months, and being a spare and delicate woman, had been greatly reduced thereby. For some time before her admission she had complained of uneasiness in her head, and said she was afraid she should go out of her mind, as her mother and

some others of her relations had done. Only an imperfect (p. 103) account could be obtained of her symptoms prior to admission, but it appeared probable that some restraint approaching to violence had been employed, since in a transient lucid interval which occurred whilst in the hospital, she expressed her satisfaction at not being likely to be again ill used. Whilst in the hospital she generally lay in a state of insensibility, almost amounting to coma, yet sometimes, in a state approaching to delirium, she would sing hymns, and try to get out of bed, but she was easily restrained. It did not appear that there was any erotic tendency in her delirium. She died six days after her admission.

Nothing remarkable was observed external to the dura mater. The vessels of the pia mater were less injected than is usual, more especially where forming the plexus choroides, which was nearly colourless. The arachnoid about the pons varolii was rather considerably but partially thickened. The substance of the brain offered nothing remarkable.

The pleuræ, lungs, pericardium, and heart were generally healthy.

The peritoneum appeared free from marks of either old or recent inflammation, and nothing remarkable was discovered in the mucous membrane of the alimentary canal.

The liver seemed healthy in form and texture, but (p. 104) its convex surface was mottled with irregular spots and blotches of a yellowish colour, which suggested the idea that the organ had received some violence.

The spleen was of its natural size and generally of a healthy appearance, but it was irregularly mottled with spots of a deeper and darker venous hue, the central parts of some of which were of a lighter colour. Notwithstanding the irregularity of these spots, they imperfectly affected a transverse direction across the organ a little above its middle. On cutting into the spleen so as to pass through some of these spots, they were found to consist of portions of the substance of the spleen indurated by coagulated venous blood, like portions of lung in pulmonic apoplexy. Some of these masses were of a light colour internally, but with little or no softening. It seems highly probable, that these appearances



in the liver and spleen, and which had in all probability nothing at all to do with the death of the patient, were the effects of some degree of injury produced by the means employed for restraint shortly after her attack.

The kidneys were not observed to offer any thing remarkable.

The uterus was of its natural size, but its lining membrane was of a deep red colour. The fallopian tubes were free from adhesions and appeared quite healthy. The ovaries were rather large, exhibited (p. 105) few cicatrices, and were remarkably smooth for those of a married female of her age. They were rather flabby.

*Example II. Extract from the report of the Case of Daniel Patrick*

In the spleen, which was rather large, there was an irregularly shaped but circumscribed mass, rather larger than a hazel nut, of a structure which at first appeared to be tuberculous, but which proved to be dependent on a peculiar alteration of structure.

*Example III. Extract from the report of the Case of J. Woodbridge*

The spleen was of moderate size; a defined portion of its structure was considerably indented, having about the firmness of liver a little indurated, the part so altered was of a light brown colour, approaching to that of new leather; the passage from this to the healthy part was abrupt, but there was no membranous separation between them. This derangement of structure did not appear to be attended with either increase or diminution of volume, so as to produce either depression or protuberance at the surface, although this was partially implicated.  
(p. 106)

*Example IV. Extract from the report of the Case of William Hunter*

The spleen was of a moderate size; it had contracted some peritoneal adhesions, there were a few small semi-cartilaginous spots on its surface, and a circumscribed portion had undergone a peculiar degeneration, by which its texture was rendered solid and of a light brown colour. As in the three former cases in which this derangement has been already noticed, it appeared, on the surface of the organ, where a slight depression existed between

the healthy and altered structure. A vessel of considerable size was seen passing through this part, which still retained some faint traces of its original structure.

*Example V. Extract from the report of James Skelton*

The spleen was of moderate size, it was in its contracted state, and its structure was generally healthy, but deeply imbedded in its convex surface, there was a light yellowish brown well defined deposit. About some portion of the surface of this deposit, there was a little extravasation of blood, apparently of an apoplectic character.

*Case VI*

October 24th, 1829. "Maria Lowther, aged 17 years, admitted into the Clinical Ward on the 22d (p. 107) instant under the care of Dr. Bright. She had enjoyed but indifferent health for some time. About five weeks ago she suffered much from a whitlow on the forefinger, caused by the prick of a needle, her finger healed, but about a week after, she appeared to have a cold. She had cough, painful respiration, and frequent rigors, she complained of great pain in the bowels and head, particularly of the latter. An abscess now appeared under the axilla, but previously to its appearance she had suffered much from irritability; this abscess dispersed, but was immediately succeeded by another on the fore-arm, together with the reappearance of the one in the axilla. Her head at this period became more confused, she grew worse, and became delirious. Her legs were observed to be œdematous on the Monday or Tuesday previous to her admission, and general tenderness was complained of for the first time yesterday. For a week past her motions had appeared bloody, and epistaxis had taken place on two occasions. Soon after her admission she appeared in an exhausted state, her face pale and anxious, her eyes sunk, and there was exquisite tenderness to the touch throughout the body. The feet and legs were slightly œdematous, ecchymosed spots were formed on the hands and feet, there was an abscess in the axilla and another on the fore-arm. The abdomen was tumid as well as tender. At night the symptoms

were aggravated, she became delirious during the night, and at the morning visit she was found in a dying state; death took place about half-past ten in the morning of the 23d."

(p. 108) The body was a little emaciated, the discolouration resembling purpura had almost entirely disappeared. The cuticle was raised both at the tip of the middle finger, and on one toe on the right side into two bullæ containing slightly purulent sanguinolent serum. The abscess in the axilla presented a cavity of about the size of a moderate orange, it was ragged internally, and of a dirty sanguinolent colour; one or more of the absorbent glands were nearly detached by the destruction of the surrounding cellular membrane.

Nothing remarkable was observed in the calvaria or membranes of the brain, except that the arachnoid was very transparent, and that there was rather an unusually small number of vessels visible in the pia mater. The substance of the brain was likewise healthy, except at the posterior part of the left hemisphere, where a portion of about an inch in diameter, occupying a part both of the cortical and medullary structure, was completely softened and broken down. It was slightly discoloured by blood imperfectly intermixed, it was not surrounded by any induration or distinct line of demarcation, but the softening was most considerable towards the centre.

Both pleuræ were healthy, with the exception of slight traces of recent inflammation at the lower part of the left lung. The substance of the lungs was likewise generally healthy, but at the posterior part of the left there were some traces of recent inflammation (p. 109) limited to a few lobules which were firmer and of a somewhat lighter colour than the surrounding structure, which was the seat of cadaveric infiltration. At the back part of the left lung there was some hepatization as well as cadaveric infiltration.

The pericardium was healthy, but contained about two ounces of straw coloured serum. There was a small opaque white patch on the anterior surface of the heart. The organ itself was quite healthy, but contained a small quantity of blood which was imperfectly coagulated, except near the origin of the vessels where

there was some coagulum prolonged into these vessels. A partial separation of the colouring matter had taken place.

The abdomen was somewhat distended, the peritoneum presented universal marks of inflammation, several convolutions of intestines were feebly glued together by tender and opaque membranous flakes of lymph. There was considerable effusion of yellow colour mixed with flocculent particles of opaque lymph, and presenting a sero-purulent character. The surface of the stomach in contact with the under surface of the liver was covered with a layer of yellow lymph. The peritoneal covering of the small intestines was easily detached from the muscular coat. The stomach and small intestines were distended with gas, their mucous membrane was generally healthy, but the patches of aggregate glands were rendered distinct by numerous minute blackish points. The (p. 110) mucous membrane of the colon was of a darkish grey colour, and was extremely irregular, which appeared to depend on lymph and other secretions becoming adherent to a number of small thickly scattered points. On scraping off this secretion, the subjacent surface presented either a smaller spot of very slight abrasion or a livid ecchymosis. This state had probably been preceded by suppressed mucous secretion. The liver was of large size, extending over the spleen to the left side, and passing down for some distance between it and the parietes. It was rather pale, but in other respects healthy, except that it presented spots of ecchymosis where it had been in contact with the spleen.

The spleen was rather large, and presented the following remarkable appearances: two portions rather more than an inch in breadth, placed transversely and occupying the whole of the shorter diameter of the spleen, were of a lightish yellow colour, they were of closer structure than the natural texture, and appeared to depend on a particular degeneration of a part of the organ itself. A process of softening had broken down the central parts of these portions, which were situated about an inch and a half from each other. The substance of the spleen in contact with these portions was of a deep livid colour and completely softened.

The pancreas was healthy. The kidneys were likewise healthy. The ovaries were of an elongated (p. 111) figure, full and plump, their surfaces presented numerous bright red points, their tunics white and dense, without any appearance of cicatrices. The vesicles of De Graaff generally clear and healthy, but a few, in one of the ovaries, were in the form of white opake semi-cartilaginous bodies. The intervening substance in both was pale, but unusually firm.

The uterus was small.

There was an equivocal appearance of a remaining hymen.

The symptoms in this case having induced a suspicion that the veins were inflamed, they were particularly examined in different parts of the body. No phlebitis was, however, discovered, yet in some of these vessels the blood was coagulated, and from its appearance had probably been in this state a short time before death.

### *Case VII*

September 21st, 1828. Martha Newton, aged apparently about 25 years, a patient of Dr. Bright's, in Dorcas's ward, into which she was admitted on the 17th instant. She had come to town from Brighton, and described herself as labouring under intermittent fever, but her appearance did not altogether accord with the idea of ague. She stated that she had been taking bark prior to her coming to town, and a repetition (p. 112) of bark or sulphate of quinine was prescribed. Her pulse was not remarkable either for quickness or irregularity, and none of her complaints suggested a suspicion of disease of any of the viscera of the thorax. She had one paroxysm shortly after her admission, which was reported by the sister of the ward to differ from the ordinary paroxysm of ague. She was seen by Dr. Bright in another of these paroxysms on the 19th. The quinine or bark was continued, but some local visceral disease rather than ague was suspected. She died suddenly on the morning of the 20th, after eating a moderate breakfast.

The body was pale and not emaciated, and rather œdematous, the areola round the nipple was but faintly discoloured. The abdomen bore no marks of parturition.

The head was carefully examined, but no morbid appearance was detected in the brain or its membranes, except some thickening, and a whitish deposit in very minute opaque particles in the plexus choroides.

There was a great deal of old pleuritic adhesion on the right side, less on the left, and a small quantity of clear but discoloured serous effusion on both sides, infiltrating the adventitious cellular structure. Both lungs had more than the natural firmness, but not the character of hepatization. They were of a (p. 113) darkish livid colour, very œdematous, contained very little air, and no tuberculous nor other deposit.

The pericardium contained two or three ounces of serum, which was very sanguinolent. This state of the serum, not only in the pericardium, but also, though in a less degree, in the pleura, was probably more the result of transudation after death than before it. There was a strong adhesion in the form of a ligamentous bridle between the close and the reflected pericardium on the left side. The pericardium on the auricle was roughened by minute elevations.

The heart appeared distended, and on being laid open by a transverse section it was found to be dilated, with thinning rather than hypertrophy of its parietes. The muscular structure was flabby and pale, and less evidently fibrous than in health. The right ventricle was nearly as much dilated as the left; no valvular disease was detected, but at the mouth of the pulmonary artery there was a singular original formation. There appeared to be four valves instead of three, a small part of one of them being cut off by a thin membranous partition.

The quantity of fluid in the abdomen was inconsiderable. There were no adhesions except in the neighbourhood of the spleen, where they were considerable, old and strong, especially between this organ and the diaphragm.

(p. 114) In the spleen there was a defined mass of about the size of a walnut of a light colour, which, as in some specimens before observed, appeared to depend on an infiltration into, or degeneration of the structure of the part. This mass appeared to be commencing the process of softening. The structure imme-

diately adjoining it was, however, much more softened, so as nearly to have effected its separation, it was of a dark or almost black colour. The remainder of the spleen, though not similarly affected, was soft, probably from cadaveric change. There was, however, one part of its substance in which a change resembling the infiltration before mentioned was commencing.

The stomach contained scarcely any food, and with the intestines appeared to be tolerably healthy.

The liver and pancreas were likewise healthy.

The kidneys were pale, and in the right there was a yellowish white mass in which a degeneration similar to that noticed in the spleen appeared to have taken place, the traces of the original structure being still visible.

The ovaries presented several cicatrices, the tubes were free from adhesions. The uterus rather large. A vascular peritoneal cyst was attached to one of the broad ligaments.







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NATHAN SMITH, M.D.

*Late Professor of Surgery and the Practice of Physic in Yale College*  
(Painted by S. F. B. Morse, Esq.; engraved by S. S. Jocelyn and S. B. Munson)

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## Nathan Smith

### BIOGRAPHY

- 1762 Born September 30, at Rehoboth, Massachusetts, of old New England ancestry. Family later moved to a farm at Chester, Vermont.
- 1780 Age 18. Became a captain in the Vermont militia, helping protect the country against the Indians. Was a teacher in the district school.
- 1783 Age 21. Watched Dr. Goodhue amputate the leg of a man in Chester and assisted by holding the leg. Expressed to Dr. Goodhue a desire of becoming a doctor of medicine, and, being encouraged, studied for a year with the Rev. Mr. Whiting of Rockingham, Vermont.
- 1784 Age 22. Became a private student of Dr. Josiah Goodhue of Putney, Vermont, for three years, receiving home and medical tuition in return for work.
- 1787 Age 25. Began practice in Cornish, New Hampshire, without a medical degree. Attended several courses of lectures at The Harvard Medical School.
- 1790 Age 28. Received degree of Bachelor of Medicine at Harvard, the fifth student in the third class to graduate from that medical school. Returned to his practice in Cornish.
- 1791 Age 29. Married Elizabeth Chase who died in 1793. The next year he married her half-sister, Sarah Chase, by whom he had four sons, Dr. David Solon Chase Hall Smith, Dr. Nathan Ryno Smith, Dr. James Morven Smith and Dr. John Derby Smith.
- 1796 Age 34. Attempted unsuccessfully to found a Medical

Institution at Dartmouth College. Went abroad to study in Edinburgh under the elder Monro and Dr. Black and in London.

- 1797 Age 35. Awarded a diploma from the Medical Society of London and became a corresponding member. Returned to America and in the Fall he delivered the first course of medical lectures at Dartmouth College, thus establishing the fourth medical College in America.
- 1798 Age 36. Appointed Professor of Anatomy, Surgery, Chemistry and Physics in the Medical Department of Dartmouth College, a position which he held until 1810. Received the degree of A.M. at Dartmouth. By 1801 forty-five men were attending the medical school but Dr. Smith's only assistant was a personally paid pupil who gave three courses in chemistry. Maintained a home and practice in Cornish and gave private instruction to medical students during the summers.
- 1804 Age 42. Received first salary of \$200. from Dartmouth College on provision that he move from Cornish to Hanover.
- 1810 Age 48. Granted \$3450. by the New Hampshire legislature to erect a medical building at Dartmouth College, provided he should "give a site for it and assign to the state his anatomical museum and chemical apparatus". In addition Dr. Smith contributed \$1217. of his own resources to complete the building. Professor of Chemistry and Theory and Practice of Medicine at Dartmouth until 1813.
- 1811 Age 49. Degree of M. D. conferred by Harvard Medical School.
- 1813 Age 51. Left Dartmouth to aid in establishing medical school at Yale University. Professor of Theory and Practice of Physic, Surgery and Obstetrics.
- 1820 Age 58. Founded, with the aid of his son, Dr. Nathan Ryno Smith, the Medical School at the University of Vermont at Burlington.
- 1821 Age 59. Established the Medical Institution of Bruns-

wick College (Bowdoin) in Maine. Professor of Anatomy, Surgery, Theory and Practice of Medicine until 1823. Performed the second ovariectomy in the United States on July 25, 1821 (he did not know that Ephraim McDowell had preceded him).

1823 Age 61. Professor of Theory and Practice of Medicine at Bowdoin College until 1826.

1824 Age 62. Wrote famous essay on typhous fever.

1829 Age 67. Died January 26 of a paralysis.

Dr. Nathan Smith is said to have been the first in the United States to perform staphylorrhaphy for cleft palate. He invented new apparatus for the treatment of fractures and originated a method of reducing dislocation of the hip.

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Physicians from the time of Hippocrates to the early nineteenth century attempted to form a satisfactory classification of the continuous fevers. Several isolated descriptions of various fevers appeared but the very words typhus, typhous and typhoid fever show how closely these conditions were related in clinical manifestations.

In 1813 Pierre Bretonneau, of Tours, gave a scientific description of typhoid fever, recognized the characteristic lesions in the lymphoid tissue of the ileum and applied the name dothiéntérite (pustule of the intestine).

In 1824 Nathan Smith, at that time of Bowdoin College in Maine, wrote the paper which is reproduced on the following pages, *A Practical Essay on Typhous Fever*. Here is one of the earliest as well as one of the clearest and most complete articles on typhoid fever. Sir William Osler held it in such high regard that, writing in *Some Aspects of American Bibliography* (1902), he says, "try to have a copy of [this essay] to hand to any young physician who asks for something good and fresh on typhoid fever."

Five years later, in 1829, Pierre Louis of Paris wrote his famous work on gastro-enteritis, using the name typhoid fever for the first time. To one of Louis' students, William W. Gerhard of Philadelphia, writing in 1837, goes the credit of first clearly differentiating between typhus and typhoid fevers. In 1842 Elisha Bartlett described the two diseases as separate entities, thus making the first clear separation. Within a few years, Alexander Stewart of Glasgow and Sir William Jenner of London had written further on the subject and laid to rest an irritating and discouraging controversy.

The second paper reprinted in this number of MEDICAL CLASSICS is Nathan Smith's famous article, *Observations on the pathology and treatment of necrosis*, written in 1827. This is one of the earliest descriptions of osteomyelitis and is remarkably clear both as to the pathology and clinical manifestations. When we consider that Nathan Smith worked without the aid of the x-ray, anesthesia or antisepsis, we must indeed marvel at the extent and depth of his knowledge.

# PRACTICAL ESSAY

## TYPHOUS FEVER.

By NATHAN SMITH, M. D.

*Professor of the Theory and Practice of Physic and Surgery  
in Yale College.*

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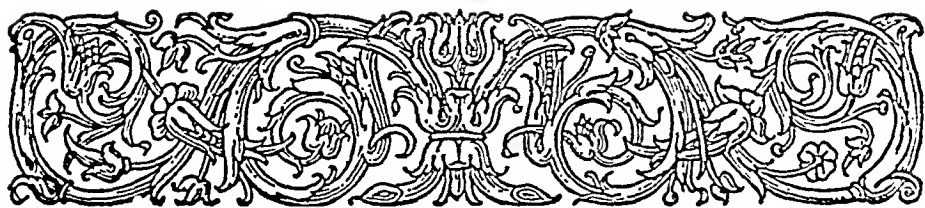
## TYPHOUS FEVER.

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TYPHUS is a word of Greek derivation, Derivation and meaning of the word Typhus. which signifies *smothered fire*, or *stupor*. As applied to disease, it is doubtful whether it was originally meant to indicate internal heat, or whether it was used to denote a fever particularly affecting the mind, and producing stupor and coma.

With regard to the history of this disease, its early history. we have no account of its first appearance; on the contrary, it is always spoken of by the older writers as an affection well known. And from the additional circumstance of its having received its name from the Greek physicians, it is probable that it has occasionally afflicted mankind from time immemorial.

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# Practical Essay on Typhous Fever

BY

NATHAN SMITH, M.D.

*Professor of the Theory and Practice of Physic and Surgery in Yale College*

**T**YPHUS is a word of Greek derivation, which signifies *smothered fire*, or *stupor*. As applied to disease, it is doubtful whether it was originally meant to indicate internal heat, or whether it was used to denote a fever particularly affecting the mind, and producing stupor and coma.

With regard to the history of this disease, we have no account of its first appearance; on the contrary, it is always spoken of by the older writers as an affection well known. And from the additional circumstance of its having received its name from the Greek physicians, it is probable that it has occasionally afflicted mankind from time immemorial.

From the descriptions given of it by European writers, there cannot be a doubt but that the disease called Typhous Fever in (p. 6) Europe and especially in England, is similar to the one known by the same name here.

I have not been able to ascertain with much certainty, at what period it made its appearance among the Europeans, who first emigrated to America. For an hundred and fifty years after their earliest establishment, there were few if any books on medical science published in this country, and no medical journals made their appearance till a still later date. Of course all we know of the diseases of that early period has been collected from historical records, which casually mention times of sickness, but give us no descriptions, or at most imperfect ones, of their appearances and symptoms.

We have reason to believe, however, from these imperfect and broken accounts, and from oral tradition, that it was not long after the first settlement of the country, before the inhabitants were afflicted with what is now called Typhus, but which was then known by the various names of long fever, slow fever, nervous fever, putrid fever, &c.

Whether the Typhous fever was originally a disease of (p. 7) this country, I have not been able to ascertain. But although I have made particular inquiries in various parts of the country, and especially near the borders of the Indian possessions, I have never found an instance of an aboriginal inhabitant having suffered from this disease.

I have likewise consulted several physicians, who have lived many years in the vicinity of Indian tribes, and who have often visited them in sickness; they have all informed me, that they have never seen a native attacked with Typhous Fever.

I do not think, however, that my inquiries have been sufficiently extensive, positively to warrant the conclusion, however probable it may seem, that Typhus has never made its appearance among them.

Whether this disease is of universal occurrence, or is confined to any particular climate or latitude, as has sometimes been suggested, is a question which I am not prepared to decide; but I have every reason to believe, that it has prevailed in every part of the United States.

(p. 8) A late writer in one of our periodical journals, has advanced the opinion, that Typhus does not prevail in the warm season of temperate climates. This conjecture is unfounded, as I have seen it attended with all its characteristic marks in every month, and, I believe I may say with truth, in every day of the year. This fact might be attested by the whole medical faculty of New England.

With regard to the liability of the two sexes, I am disposed to think there is not much difference in the number of each attacked, but more females are cut off by it than males, in consequence of its appearance during pregnancy and soon after parturition.

As to age, I have never seen a child nursed at the breast affected with it, but other physicians have; and those in whom I could

place confidence have assured me that they have met with infants suffering under this disease; and if so, it may be said to attack both sexes and all ages, from the cradle to the grave.

Notwithstanding its general occurrence throughout the country, long periods of time (p. 9) have elapsed, in which it has not existed in particular sections of country of considerable extent.

When I commenced the practice of physic in 1787, in Cornish, N. H., a town situated on the banks of the Connecticut river, I was informed by physicians, as well as the inhabitants who had resided many years in that part of the country, that about twenty years previous, a fever, which they had called *nervous*, had prevailed in that vicinity,—had soon after disappeared, and, for the twenty years next succeeding, had not returned in a solitary instance. It was eight years after, during which time I visited the sick pretty extensively in that and the adjacent towns, before I saw or heard of a single case of Typhous Fever. I was then called into a family, one member of which had died of this disease, and another then lay sick of it. Soon after, I left this portion of country, and was absent for about eighteen months, and was in consequence unable to trace the course of the disease; but in 1798, a year after my return, it made its appearance in the village surrounding (p. 10) Dartmouth College, twenty miles distant from Cornish, and in several neighbouring towns simultaneously. From that time to the present, a lapse of more than twenty-five years, I have never so far lost sight of the disease, as to be unable to follow its changes from one place to another, and to tell where it was prevailing.

During this same period, it has appeared in all the New-England states, and as far west as my knowledge extends. Indeed it seems to possess a migratory character, and travels from place to place, and, after remaining in one village for a longer or shorter time, as, from one year to two or three, it ceases and appears in another.

I have not observed that situation has any influence either in producing or preventing this disease. It affects alike persons living on mountains and in valleys, on plains and the banks of rivers, and on the borders of lakes and stagnant ponds.

And I have not perceived that occupation or habits of life make

any difference in their liability to receive this disease, nor has it in (p. 11) this country been confined to the poor and filthy; but affects nearly alike the rich, the poor and middle classes.

That the Typhous Fever is contagious,\* is a fact so evident to those who have seen much of the disease, and who have paid attention to the subject, that I should have spared myself the trouble of saying anything with regard to it, did I not know that there are some physicians in this country, who still dispute the point; one, which I think can be as fully demonstrated, as that the measles, small-pox, and other diseases universally allowed to be contagious, are so.

The arguments usually brought against this opinion are, that in certain cases, we cannot trace the contagion to its source, and that many persons exposed to it, do not contract the disease. These objections might be advanced with equal truth against the contagiousness of all diseases; as it frequently (p. 12) happens, that one or more individuals in a family will escape an attack, though equally exposed as those who suffer from it.

A few instances, which have fallen under my own observation, would alone be sufficient to determine the question.

A young man, a pupil of mine, was attacked with the Typhous Fever, from which he recovered with difficulty. Some of his family, who lived about forty miles distant, came and took care of him during his sickness. Upon his recovery, they returned home in good health, but soon after sickened with the same disease, and communicated it to others, who had not been exposed in the first instance. From this, it spread to numerous other families in the vicinity, who had been exposed to the contagion. In the whole town where this occurred, there had been no case of Typhous Fever for many years, till brought there by the circumstances above related.

During the prevalence of the Typhous Fever in Thetford, (Vt.) a woman went there from Chelsea, about ten miles distant, to visit and administer to a sister sick of this disease. (p. 13) Upon

\* Without going into a discussion upon contagion and infection, I would observe, that by a contagious disease, I mean simply, one that can be communicated from one individual to another.

her return, she was herself attacked by it and soon after died. Others of her family contracted it of her; and in about four weeks, there were thirty persons taken down with Typhus, all of whom had been exposed to the contagion.

A young man belonging to Plainfield, (N. H.) who had left his friends, and resided for some time in the western part of the state of New York, returned to his father, who had a numerous family. He found himself unwell before he reached home—was immediately confined with Typhus, and soon sunk under the disease. In about four weeks after, I was called into the family, and found nine members of it sick of the same fever.

With a knowledge of these facts, and many more, equally to the point, it is impossible for me not to believe this fever contagious, though it may not perhaps be so certainly and readily communicated as some other contagious diseases.

Some physicians admit that Typhous Fever is often communicated from one person to (p. 14) another, who nevertheless suppose that it is frequently produced without any contagion or specific cause; that is, that it arises in many cases from errors in diet or exercise, from the effects of temperature, or what Sydenham would call an epidemic state of the atmosphere, from marsh miasmata, or confinement in close and crowded apartments. This is a difficult subject, and it is not easy to demonstrate that it is never produced by some or all of these causes, and perhaps the circumstance of analogy is all that can be adduced against the assumption.

However, the fact already noticed, of the absence of Typhus in a large section of country, for an interval of more than twenty years, would lead us to doubt the possibility of its being produced by any of the accidental causes above enumerated; for in such an extent, and among so many people, it is impossible but that some of these circumstances should have occurred—and the disease of course be produced. Besides, if it can be communicated from one person to another, it has a specific cause, and I know no disease (p. 15) that arises from a specific cause, that can be produced without the agency of that cause.



It has been suggested that Typhus occasionally arises from marsh miasmata,\* the same which under certain circumstances, produce intermitting and remitting fevers. A fact, which I shall here adduce, is strongly opposed to this hypothesis. On the Connecticut river, from Northampton, in Massachusetts, to its source, a distance of more than two hundred miles from north to south, and on all its tributary streams, on both sides, for an hundred miles in width; there has been no instance of any person's having contracted the intermitting fever, from the first settlement of the country to the present time; and yet the Typhous Fever has prevailed more or less in every township within that tract of country.

The Typhous Fever, as far as my experience, which has been considerable, enables me to judge, is a disease *sui generis*, exhibiting as little variety in the different individuals affected by it, as some of the diseases which (p. 16) are acknowledged always to arise from contagion. If its duration is not so uniform as some of the contagious diseases, it is less irregular than others, which spring from specific causes, as for instance the intermitting fever.

There is another marked point of analogy between Typhus and the common contagious maladies, which is, that it rarely affects the same individual twice. Those, however, who do not consider it a distinct disease, but only a state of fever, will probably differ from me in opinion on this point. For it is evident, that if we make the name of the disease depend on the presence of one or two symptoms, or on that indefinite thing or state called debility, we shall be liable to misname it, and that this is actually done, and in very many instances, there can be no doubt. Indeed, within the last year, I have been consulted in several cases of disordered secretions of the digestive organs,† which were called low (p. 17) nervous or low typhous fever, merely on account of the presence of a furred tongue, loss of appetite, and some degree of thirst. Several of these patients told me, that they had had

\* Good, Study of Medicine, Vol. II, p. 188.

† "Acute disorder of the digestive organs" of Hall—On Diagnosis, part 2, p. 102.

one of those "low fevers" every year, for several years in succession. It is obvious that those physicians who have such vague and indefinite notions of fever, as to call a stomach affection, Typhus, would be equally liable to call other febrile complaints by the same name, and may imagine they detect its existence in the same individual many times.

My own personal experience is strongly in favour of the opinion I have advanced of the non-liability of the same individual, to a second attack of Typhus; for during the twenty-five years since I first attended patients in this disease, and in that time I have visited many hundreds, and have witnessed its prevalence several times in the same village, I have never known nor heard of its recurrence in the same person.

I once attended a numerous family, every member of which was sick of Typhus, except two, who escaped at that time; but two years (p. 18) afterwards, when the disease again appeared in that neighbourhood, those two individuals of the family, and those alone, were attacked.

In another family, which I attended, consisting of eight persons, five of the eight had the disease during the autumn, and early part of the winter, and recovered. The next summer, the remaining three and another person, who had been added to the family after the former sickness, were attacked by it, while all those previously affected escaped.

The experience above spoken of, in addition to these cases, and numerous others equally in point, forms a strong presumptive proof, that in this respect, there is an analogy between Typhus and the common contagious diseases.

Some later writers, have described a fever beginning inflammatory, and ending typhous, and vice versa. Upon this point, I would observe, that in many if not all acute diseases, there is a marked difference in appearance between the rise and decline of the same (p. 19) disease, whether it terminates in death or recovery, and generally, the early part of all febrile affections is attended with more symptoms of inflammation than the latter.

This is undoubtedly the case with Typhus; but such difference of symptoms in its different stages, should not induce us to give the disease different names.

As I consider Typhous Fever as arising from a specific cause, if it begins Typhous, or arises from such specific cause, I believe it to continue Typhous through its whole course. Variations, in severity or mildness, can make no specific difference in the disease.

With regard to the combination of Typhous fever with other diseases, the opinion has been often, and confidently advanced, that two diseases arising from specific causes could not exist in the same individual, at the same time. But however dogmatically it has been stated, it is nevertheless without foundation, since I have myself seen the Hooping-Cough, and the most malignant dysentery (p. 20) coexisting in the same person.\* It has been stated by Mr. Harty,† that Dysentery and Typhous Fever often combine, and I can add my testimony to the same fact, for I have often seen a patient taken sick with all the characteristic marks of Dysentery, and after some time the dysenteric symptoms have wholly subsided, while those of Typhus have continued for many days, so strongly marked as to leave no doubt on my mind of the truth of Mr. Harty's position.

I have likewise often seen this disease attack persons under the influence of epidemic (p. 21) catarrh, and the symptoms of both diseases continue perfectly evident for some time.

From the view of this subject above taken, and the facts there stated, I consider Typhous Fever a disease *sui generis*, arising

\* Extract of a letter from Daniel Sheldon, M.D. of Litchfield, Conn.:

"In the course of the year 1807, the mumps, hooping cough and measles were all prevalent in this town, at the same time. The children of the Rev. Dan Huntington, then a resident here, were subject to these complaints. One of them had the mumps, hooping-cough and measles at the same time; another, the measles and one of the other complaints, which I do not now, accurately remember. In each child, the peculiar symptoms and appearances of each disease were exhibited and strongly marked; and, so far as I observed, progressed together, without any mitigation or suspension of either. Each of the children, after the abatement of their disorders, had an inflammatory swelling about the neck, of considerable size, which suppurated and was opened."

† Observations on Dysentery and its combinations, by William Harty, M.B. London, p. 57, et seq.

from a specific cause, and that cause contagion, and seldom affecting the same person more than once.

The diseases with which it is liable to be confounded, and for which it is often mistaken, are pure unmixed catarrhal fever, the acute stomach complaints above referred to, and those bilious affections, which take place in the latter part of summer, and the commencement of autumn.

I have seen many cases of all these affections, which have been considered and treated as Typhus, by those who consider it as a mere state of fever, and not as a distinct disease, dependant on a specific cause.

It will be observed, that simple inflammatory fever is not mentioned as one of the diseases with which it may be confounded. The reason is, that no such disease has ever fallen under my observation.

(p. 22) Although I have practised physic and surgery for thirty-five years pretty extensively in all the New England States, except Rhode-Island, and have lived in New-Hampshire, Vermont, Connecticut and Maine, I have never witnessed a single case of continued fever, except Typhus, which was not either the effect of contagion, as the small-pox, measles, &c. or evidently connected with local inflammation, and dependant upon it.

I do not mean to assert that Typhus is never connected with local inflammation; indeed I know that the reverse of this has been the opinion of some men of great observation, and that there are many phenomena, which serve to corroborate it; but if so, it differs essentially from that kind of sympathetic fever, attendant on phlegmonic inflammation, and on attentive examination, this difference will be sufficiently obvious.

Typhus, like the other contagious diseases, has a natural termination, and if it does not end fatally when uninterfered with, it gradually exhausts itself and disappears; (p. 23) at the same time, unlike those diseases, it is not restricted in its duration to so narrow limits.

So far as I have observed, it has rarely terminated under fourteen days from its commencement, and seldom exceeds sixty.

In a few rare instances, it may have terminated earlier or continued later. In one case I visited, the patient had been confined an hundred days, and the symptoms still resembled Typhus, but the specific character had probably been changed, and these symptoms were rather the effect of the disease, than an evidence of its then actual existence.

With regard to the remote and proximate causes of this fever, which have been so often and diffusely described by the learned, if the remark made above be correct, contagion may be considered as the antecedent to all which follows its application, and that without it, no effect would be produced. But how this cause operates upon the system, or on what part it makes its first impression, (p. 24) or how this first impression produces the ultimate effects, we are wholly ignorant. As for the proximate cause I know not how to separate it from the disease itself. Since the disease is known only by the phenomena it exhibits, these phenomena may be considered as constituting the disease, or all we know of it.

According to our late nosological arrangements, the Pyrexia, or febrile diseases, affect principally the circulatory system; if so, the affections of the other functions, are the consequence of the change first induced in this system. But as all the different parts of this system, are destined to perform different functions, it may happen that a disease may primarily affect one part only, and the change produced in the rest of that system, may be the consequence of a change produced primarily, in another part.

In the sanguiferous system, the proper function of the heart seems to be nothing more than to receive the blood from the veins, and throw it into the arteries, which may be considered as living canals, intended to convey (p. 25) the blood from the heart to the system of capillaries. Here all the functions belonging to this system are performed, such as nutrition, reparation of the body, absorption, secretion and the production of animal heat. Of course, the functions of the heart and great arteries must be

considered wholly subservient to those of the capillaries, which in reality, perform all the great and essential offices of the circulating system.

As this fever is supposed to make considerable change in the action of the circulating system; the question presents itself, what part is first affected? does the increased action of the heart and great arteries, cause the increased action in the capillaries, or *vice versa*?

In cases of local inflammation, which produce symptomatic fever, it appears very evident that the capillaries are first affected; the action of the heart and great arteries is not changed till symptomatic fever is produced; and that this symptomatic fever, seems to commence in the capillaries, is evinced (p. 26) by the paleness of the skin, and the chills with which its first appearance is accompanied.

The analogy between the inflammatory and febrile action is so great, that we may with confidence rely on the similarity of cause.

The paleness of the skin, and the sense of cold spoken of above, which attend inflammation, and precede the attack of fever, or the development of those phenomena to which we usually apply the name, and which is followed by an increase of the action of the heart and arteries, I explain in the following manner. Before the diseased action can take possession of the capillary vessels, the natural and healthy one must cease, unless disease is a mere increase of the healthy action, which we have abundant reason to believe is not the case. It is during this interim, that is, between the interruption of the natural healthy action, and the complete establishment of the diseased one, that the patient feels the chill.

Something of this kind is observed in cases of local inflammation, which still continues (p. 27) to extend itself. A few lines beyond the discoloured part of the skin, between that and the portion which still retains its natural tint, there is a pale circle, evidently showing that the action of the capillaries in that part is suspended.

When local inflammation proceeds so far as to produce symptomatic fever, a degree of paleness accompanied by chills, precedes the increase of heat.

Upon the whole, whether we consider Typhous Fever as dependant on local inflammation or not, it is probable, nay, it is very certain, that like all other febrile diseases, the morbid action commences and continues principally in the capillary system, and that the change which we perceive in the action of the heart and great arteries, is symptomatic of the disease existing in that system.

The most violent affections of the heart and large arteries, as in palpitation, do not produce the slightest symptoms of fever, which serves to show that these two parts of the circulating system have diseases as distinct (p. 28) and different from each other, as their functions.

The symptoms of this disease, may be divided into such as affect the functions of animal life, and those of organic life.

The changes produced in animal life, may be referred to affections of the mind, of the organs of sense, sensibility and voluntary motion.

Those occurring in organic life, to changes produced in the respiratory, circulatory and digestive systems, to secretion and excretion generally, together with its effects on the animal heat.

Amongst the earliest symptoms belonging to the first class, are dull, aching pains in the head, back and limbs, usually commencing in the head and back, but in some cases in the lower extremities, attended generally with a sense of lassitude and fatigue. The patient's flesh, as they often express it, is very sore.

The symptoms, as they appear in the nervous system, are a disinclination to make any mental exertion, forgetfulness, inability to (p. 29) measure time, total incapacity to pursue any train of thought, or to attend to business. As the disease advances, delirium often makes its appearance, sometimes continuing day and night, at others, it is present in the night only. In a still more advanced stage coma supervenes, but not often so profound that the patient cannot be roused from it by speaking loud to him,

although upon ceasing to speak he immediately falls back into the same state.

In a few instances I have known patients in their delirium impressed with an idea of some persons having abused them; and this idea has continued till after they have recovered, and even then obliterated with difficulty.

In two cases which I have met with, instead of delirium, a kind of insanity appeared pretty early in the disease; and in both, as the insanity came on, the peculiar symptoms of Typhus abated.

In one instance it was of a playful childish nature, in the other there was a display of great wit and humour.

(p. 30) In both it continued about four weeks, and as it then gradually subsided, a restoration to health took place.

There is in this disease not only a forgetfulness of the lapse of time and of occurrences that have recently happened, but though the patient appears sensible, and gives rational answers through the whole course of the disease; yet after his recovery, the whole time elapsed, and all the circumstances that have taken place during that period, are entirely blotted from the memory, and are never after recovered.

The hearing is often impaired almost from the commencement of the attack. Sometimes false hearing occurs, and the patient imagines he perceives voices and sounds when nothing of the kind exists.

The sense of vision is not so much impaired as that of hearing; and blindness, I believe, never occurs till near the point of dissolution. But false, double, and distorted vision sometimes arises.

To an observer, the eyes present a peculiarly heavy and languid appearance and are (p. 31) a little watery, but in the beginning of the disease, there is not much evidence of inflammation. The red vessels however on the conjunctiva are often a little enlarged, and appear more numerous than in a state of health. In the latter stage they become more turgid and of a darkened colour.

The secretions of the mucous membrane of the eye are often considerably affected, become thick and viscid, and accumulating in its angles, dry and put on the appearance of scabs.

There is sometimes a considerable increase of sensibility to light.



The voluntary motions are unsteady, the tongue trembles when an attempt is made to protrude it, and the patient's hand shakes when he attempts to bring it to his head. There is often more or less starting of the tendons, and the muscles of the face are agitated, especially when asleep, so as to produce momentary distortion.

The voice is altered, from the beginning. Early in the disease it is usually rather plaintive and small, but as it advances, and more (p. 32) particularly in bad cases, it becomes guttural, and at last truly sepulchral.

The patient is generally inclined to lie on his back, and he insensibly slides down toward the foot of the bed.

It has appeared to me in some instances that the moral principle has been affected. One patient in particular, who had been extremely sick with this disease, after his recovery had a strong propensity to steal, and did in effect take some articles of clothing from a young man to whom he was under great obligations for the care he had taken of him during his sickness. He at length stole a horse and some money, was detected, and punished. I took some pains to inquire into the young man's former character, and found it good, and that his family were respectable.

The symptoms of Typhus indicating a disturbance of the functions of the circulatory system are an increased frequency of the pulse, without fulness, or usually any considerable degree of hardness, from the commencement of the disease.

(p. 33) The pulse is generally rather easily compressed, and when the disease is severe, has often a peculiar, undulating stroke or a second small beat following each full one.

The animal heat is always deranged in this disease. In the commencement, there is generally some degree of chilliness felt by the patient, although his skin feels warm to the touch. This sense of cold often continues at intervals for three or four days.

The heat on the surface of the body varies in intensity at different times of the day, and is greatest during the exacerbations, of which there are generally two in the course of twenty-four hours. They do not however appear regularly at the same hour each day, but vary both in the times of their appearance and in their severity.

In the commencement of the disease the most marked exacerbation occurs oftenest in the evening.

The heat is ordinarily very unequally diffused over the body; sometimes the head and trunk will be excessively hot, while the extremities are cooler than natural; at others, (p. 34) the extremities will be preternaturally hot, when the body is but moderately so. One cheek will often appear a deep red colour and be very hot, while the other remains pale and cool; as its colour and heat subside, they seem to cross over and affect the opposite cheek in the same manner. This colour and heat usually extend so far as to include the ear of the affected side.

Haemorrhage is not an uncommon symptom in this disease. In a majority of instances in which it takes place, it arises from the intestines, not unfrequently from the nose, and more rarely from the kidneys.

In females of adult years it is often from the uterus.

This symptom is most apt to show itself at about the height of the fever.

Livid spots occasionally appear on the skin, and blistered surfaces sometimes become black and gangrenous.

The effect of Typhous Fever on the secretions is sudden and universal; they are all changed either in quantity or quality from the very commencement.

(p. 35) The saliva is generally diminished in quantity, becomes glutinous and produces great thirst; but in some cases its secretion is augmented and the patient spits great quantities of frothy mucus, without any desire to take liquids as in the other case.

The tongue in the commencement of this fever is covered with a white fur, which as the disease advances assumes a yellow tinge, and from that gradually changes to a brown, which eventually becomes almost black. Arrived at this state, it cracks and peels off, leaving the tongue smooth, dry and very red. It is then again renewed and again comes off, making these changes, in severe cases, several times in the course of the disease.

The teeth are often incrustated with a brownish matter, which adheres to them closely near the gums.

The fauces are covered with a thick tough mucus, which is sometimes thrown off in large quantities.

The urine is changed both in quantity and quality. In the commencement of the fever it is not high-coloured and is considerably copious, (p. 36) being often above the natural quantity, and deposits no sediment. In voiding it into a vessel it often foams like new beer. As the disease advances, the urine becomes more highly coloured, and as it begins to decline, lets fall an abundant sediment. In very severe cases, the patient evacuates his bladder but seldom, allowing the urine to accumulate there in very large quantities.

The changes produced in the functions of the digestive apparatus are a vitiated taste, want of all appetite and desire for food, and a total loss of the power of digestion in the stomach. Sometimes nausea and vomiting take place; whether this last is spontaneous or produced by art, the matter discharged shows, that the secretions of the stomach are entirely changed.

Sometimes, the matter thrown up consists wholly of vitiated mucus, at others, it is mixed with bile of an unhealthy colour and consistence.

The peristaltic action of the intestines is sometimes suspended and at others preternaturally increased, and whether the stools (p. 37) appear naturally or are solicited by art, they are always liquid, generally of a dark colour and have an unnatural and excessively fetid odour.

The latter stage of all severe cases of Typhus is attended with diarrhoea; the stools are frequent, copious, liquid and extremely foetid. The bowels are often tympanitic, the flatus not passing off with the liquid stools.

The danger of the disease is in proportion to the violence of the diarrhoea; when the patient has not more than four or five liquid stools in the twenty-four hours, it is not alarming, as it does not seem to weaken him much, but if they exceed that number, serious consequences may be apprehended.

I have never lost a patient, whose bowels continued constipated through the whole course of the disease, and have never known a fatal case of Typhus, unattended by diarrhoea.

The respiration is always affected in a greater or less degree. There is generally a correspondence between the state of the

respiration and that of the pulse, which is (p. 38) frequent and undulatory, when the breathing is hurried and unequal, or accompanied, as it frequently is, by occasional long and full inspirations like sighing.

After the patient has been sometime sick, if the disease proves severe, there is a peculiar whistling sound produced when he breathes through the nose, and when asleep or lying in a state of coma, the mouth is generally kept open and the breathing has somewhat of a stertorous sound.

In some instances, there is no sensible perspiration for several days succeeding the attack of the disease, in others, there will be more or less sweating about the head, face and superior part of the body, while the other parts remain dry and hot.

Occasionally, the patient will sweat, during a part of the twenty-four hours, almost from the beginning of the fever.

In fatal cases there sometimes appears, what has been called the *washer-woman's sweat*, which is extremely profuse over the whole surface of the body and extremities, standing in large drops on the face, and giving (p. 39) to the cuticle, on the palms of the hands and soles of the feet, a corrugated appearance and a light colour, as if it had been long macerated in water. In such cases, the perspiration is warm till a short time before the patient expires. I have never seen an instance of recovery after this kind of sweating.

After the fever begins to decline, the perspiration becomes universal, especially while the patient sleeps; in this case it is not very profuse and produces a cooling and not unpleasant effect.

The skin has a peculiarly dirty appearance, and feels harsh and dry except when covered with perspiration. In some instances the surface of the patient's body communicates to the touch a sense of scalding, or a certain kind of pungency, which is difficult to describe, but, when we are accustomed to it, readily distinguished from the sensation given in any other fever, which would perhaps equally affect the thermometer.

In the advanced stage, it is not uncommon for boils to appear; if they have a bright red colour and proceed to suppuration, it is a favourable symptom. (p. 40) Sometimes there appear erup-

tions about the mouth, these are considered by most physicians as a good indication, and I think I have generally found them so.

There is a remarkable odour arising from a person affected by this disease, so peculiar that I feel assured that upon entering a room, blindfolded, where a person had been confined for any length of time, I should be able to distinguish it from all other febrile affections. This is an additional circumstance in favour of the existence of the specific cause assigned above; as several other diseases which arise from contagion are attended by an odour peculiar to each, which, when once fixed in the mind, enables a person to recognise their presence ever after. This is strongly evinced in small-pox, measles, malignant sore throat, &c.

The absorbent system is perhaps less affected than any other, in consequence emaciation takes place rapidly. This is rather a good symptom, for I have observed that patients who emaciate rapidly are more likely (p. 41) to recover, than when they retain their ordinary degree of fatness, or when the face appears full and bloated. This last symptom, occurring after the disease has existed some days, indicates great danger.

In some instances, the power of absorption in one of the lower extremities is in a degree lost, and one leg and thigh become enlarged. As the fever abates, the cellular substance appears to be loaded, the muscular power is weakened, and the limb feels heavy and unwieldly.

In some cases, it is eventually restored, in others, the enlargement continues through life.

After the fever has subsided entirely, and the appetite is perfectly restored, the patient generally gains flesh very fast, and often acquires a greater size and weight than he possessed before the attack.

This increase in size takes place much earlier and more rapidly than the acquirement of muscular strength.

In cases where the disease has been very severe and the patient has recovered, the hair (p. 42) comes off from the head, and is succeeded by a new growth; this happens more frequently with those who have much and long hair. The new hair, however, never acquires so great a length as the old.

After a very severe attack, the cuticle peels off from the palms of the hands and soles of the feet, and sometimes from the whole surface of the body; as is perceived when the skin is rubbed by the hand when in a state of perspiration.

The cuticle never separates in this way till the diseased action diminishes and the patient begins to recover.

As it respects critical days, much has been said and written from the earliest physicians to the present time; for my own part, I have never been able to determine that any exist, or if there are, they can be of no use, in a practical point of view, for two reasons; first, the disease attacks in such a gradual manner that we hardly know on what day to fix its commencement; and second, when it terminates favourably, it often happens that the patient (p. 43) remains a week or more in such a situation that the practitioner is unable to decide, whether he is mending or failing.

If the pathology of Typhous Fever we have just laid down, be correct, if it arises from a specific cause and has a natural termination, it may be a question, how far we are to attempt a cure of it, or if we possess the power, whether we can with propriety cut it off in its commencement and by art prevent its running its course.

Physicians in this country are divided in opinion on this subject, some imagine they have often cured it immediately after its first attack, nipped it in the bud, as they say, while others of perhaps more experience will tell you they are not certain they have ever arrested this disease by medicine.

I confess the subject is a difficult one, and that it is next to impossible to demonstrate the truth of either the positive or negative side of the question, and as absolutely so to those who have already made up their opinions on (p. 44) the subject, as to that still larger class, who have yet to learn to doubt their own skill and mistrust the powers of medicine.

When a person is taken unwell, he has a pain in the head, takes medicine, and the next day recovers, if the attending physician is disposed to consider it a case of Typhous Fever, we can bring no testimony to prove that he would not have had the disease, had he not taken the remedy.

In such cases we can only make the truth probable, and what appears so to one, may not to another.

In the first place, Typhus in its commencement exhibits so many symptoms in common with other febrile affections, that is not easy for any one, especially the unexperienced, to determine whether the disease is truly Typhous or not; even those, who hold to the opinion that they often cure it suddenly, have confessed to me that they cannot distinguish it from other febrile affections upon its first attack, and never positively, till the disease has, in a considerable degree, developed itself.

(p. 45) This confession is alone sufficient to render the correctness of their previous opinion doubtful.

Again, these very physicians, or at least a portion of them, have acknowledged that when the disease is fully formed, that is, when the patient has the Typhous Fever, it cannot with any certainty be interrupted or cut off, as they express it.

Besides, we have to oppose to the opinions of those, who think they often cure this disease in its commencement, the belief of others of quite as much experience, who think they have never interrupted its course in a single instance.

Indeed, I am myself of this latter opinion, for during the whole course of my practice I have never been satisfied that I have cut short a single case of Typhus, that I knew to be such; nor have I seen a solitary instance of its having terminated within fourteen days from its first attack.

Cases have occurred to me often where the distress and sufferings of a patient have been alleviated in less than half that time; but the (p. 46) morbid action has not ceased, nor the healthy one of the secreting surfaces been established, and a natural appetite restored, within the time above-mentioned.

It does not follow, because we have no expectation of arresting the disease, that we are to neglect doing any thing. In cases of the other contagious diseases, which are destined to run a certain course, as the small-pox, we often prescribe early in the disease, and with evident good effect, but not with a view to stop or cut off the disorder; for whatever we do, we expect it will pass through all its regular stages, and our prescriptions are calculated only

to render it milder and safer, and enable the patient to live through it.

With the same views, I prescribe for Typhus, both at its commencement and through the course of the disease; for Typhus has a natural termination like other diseases, which arise from specific causes.

On the other hand, it does not follow of course, that this disease in all cases requires remedies, or that a patient should necessarily take medicines because he has the disease. (p. 47) In other specific diseases, we proceed on the principle of withholding our remedies unless they are called for by particular circumstances, and thus many cases of measles, whooping-cough, and other contagious diseases go through their course to their natural termination without medicine.

In cases where the disease is going on regularly in its course, without any symptom denoting danger, and without any local distress, it is presumably that medicines, especially powerful ones, would be more likely to do harm than good. Although Typhous Fever is a more formidable disease than measles or whooping-cough, yet there are many mild cases, and in such cases, I apprehend that the use of powerful means, with a view of curing the disease, is liable to do great mischief.

I have seen many cases, where persons in the early stages of this disease were moping about, not very sick, but far from being well, who, upon taking a dose of tartrate of antimony with the intention of breaking up the disease, have been immediately confined to their beds.

(p. 48) In fact, I feel well convinced, that all powerful remedies or measures, adopted in the early stage of Typhous Fever are very liable to do harm, and that those patients, who are treated with them in the beginning, do not hold out so well in the latter stages of the disease.\*

\* Happening in company with a physician with whom I was slightly acquainted, he observed that he had adopted a new method of treating Typhus, which I was aware had been prevalent in the vicinity where he lived, and stated that it had proved very successful. Upon my inquiring into his peculiar mode of treatment, he informed me that it consisted in giving his patient milk and water, and nothing else, through the whole course



If it is determined that something must be done at or about the commencement of the disease, the question is, what that something shall be, and the first thing usually suggested is blood-letting.

From the time Dr. Cullen published his "First lines of the theory and practice of Physick," till very lately, students were generally taught to believe, that Typhous Fever was (p. 49) produced by some weakening power, and was, in effect, a disease of debility.

Dr. John Brown enlarged upon this theory, and inculcated a notion in accordance with it, that it should be treated by the most powerful stimulants. He considered bleeding and all other modes of depletion as highly reprehensible, because Typhus was placed at the lower end of his scale of diseases, that is, below the standard of health.

This theory was carried into practice by many, and those, who might not have been converts to Brown's peculiar doctrines, not having sagacity enough to perceive that this debility was the same thing as specific disease, were nevertheless cautious about bleeding in a fever, which they considered Typhus, or possessing what they called a Typhous type. The most approved English authors since Cullen have held this doctrine till within a few years.

Very lately several writers\* have ventured to recommend bleeding in this disease.

(p. 50) Some of them have advised this practice in certain cases, where there appeared to be more than an ordinary degree of excitement in some particular organ, in the brain or lungs for example, while others have recommended it, simply because the disease was Typhus, without waiting for any particular symptom, or set of symptoms to indicate its necessity.

The practitioners of medicine in New England, have been divided on this subject; and while one part have become converts

of the disease, and affirmed that he had treated quite a number of patients, and had not lost a single one since he had adopted this mode of treatment.

I take this to be a confirmation of my opinion, that powerful remedies are not properly used in this disease, unless called for by particular circumstances, and these circumstances are more rare than is generally supposed.

\* Armstrong, Pritchard, &c. &c.

to the doctrine of blood-letting to a high degree in this affection, the other have condemned it *in toto*, and, as though opposition had produced a kind of reaction on their part, they have had recourse to the most powerful stimulants both internally and externally, such as opium, wine, alcohol, and the most acrid stimulants, as Cayenne pepper, arsenic, &c. Indeed, individuals of this latter class have carried their prejudices to such an extent, as even to boast of having made their patients swallow three pints of strong brandy, accompanied with large doses of laudanum and cantharides.

(p. 51) I have myself seen a written prescription, in which opium, wine, alcohol, cantharides and arsenic, were all directed to be taken several times in the course of twenty-four hours.

It is remarkable, that though the practice of these two sects, for such they seem to be, is as opposite as possible, each considering the other's mode of treatment as highly deleterious, yet all boast of success and enumerate various cases, which have fallen under their care, with scarcely the loss of a single patient, yet notwithstanding these two highly improved modes of treatment, it is a notorious fact, that Typhous Fever often proves fatal.

There are but two ways of accounting for the equal success of these two opposite modes of cure, for as far as I can judge there is not much difference in the success, which attends them, either the disease is not so much under the control of blood-letting as they would have us believe, or these two extremes produce about an equal degree of mischief; for it is not conceded, that if a patient does not require (p. 52) bleeding, he stands in need of opium, arsenic, cantharides, or alcohol.

It has been observed that in certain cases of Typhus, there is great pain accompanied with a sense of fullness in the head, and in other cases, the patient complains of severe suffering in the chest, which is increased by a full inspiration.

Under these circumstances, the loss of blood, to the amount of from twelve to sixteen ounces, often mitigates these troublesome symptoms, and probably may not only alleviate the patient's suffering, but may enable him to go through the disease with more safety.

So far as I can judge from my own experience, bleeding does not

generally produce any considerable change in this disease; the pulse is not rendered slower by it, and after the faintness, if there is any produced by the operation, disappears, the heat is not perceptibly diminished.

In some cases, in which I have resorted to this expedient, I feel confident that the pulse became more frequent and the temperature (p. 53) of the body higher, in consequence of the loss of a pound of blood.

As haemorrhage sometimes makes its appearance in Typhous Fever, and generally at about the height of the disease; the advocates for indiscriminate bleeding have imagined that taking blood early in the disease will prevent its occurrence. Upon this subject little need be said, since it is next to impossible to disprove the assertion; for my own part, I have never seen any evidence of its truth.

In the autumn of 1812, Professor Perkins, now of New York, and myself, attended between fifty and sixty cases of Typhus in the vicinity of Dartmouth College, and many of them students of that institution.

Of the whole number, which came under our care, only one was bled, and that on account of a sense of fulness in the head, of which he complained.

This patient had afterwards a haemorrhage from the bowels, which was pretty profuse, but he eventually recovered.

(p. 54) This symptom did not occur in any other of our patients, of whom we lost but one.

I am sensible that it is not safe to rely on one fact alone in making up an opinion on a practical subject. This case is mentioned only to show that bleeding does not always prevent haemorrhage; and from the success of our practice, it would seem that blood-letting is not so essential, as some would persuade us to believe.

That patients often recover from this disease after blood-letting has been practised is an unquestionable fact, and the inference which should perhaps be drawn from it, in conjunction with the facts mentioned above, is, that the loss of a moderate quantity of blood in Typhus, is not of itself dangerous, and in a majority

of cases, may be allowed with impunity. There are cases however in which it may be essential to the patient's safety, while in others it may prove highly injurious. The judgment and skill of the physician is necessary in each individual case to determine the propriety of its adoption, as well as the quantity which should be abstracted.

(p. 55) I have never seen any benefit from blood-letting in Typhous Fever, where there was no local inflammation or congestion, that particularly called for it.

The symptoms, which would induce me to bleed, are uncommon pain in the head, accompanied with great heat in that part, a sense of fulness, and a throbbing of the temporal arteries, or marks of congestion in the viscera of the thorax, such as pain in one or both sides of the chest, increased by a full inspiration.

The state of the pulse also should be considered before we bleed; a very frequent one does not indicate blood-letting, on the contrary, in such cases I have seldom or ever seen this evacuation attended with advantage.

Many of the French physicians prescribe leeches instead of general bleeding, and where they can be procured, the remedy may be tried with safety, as there is less to be apprehended from the loss of an equal quantity of blood by leeches than in any other way.

The blood, drawn in Typhus, seldom shows a buffy coat, and as far as I can judge, is found (p. 56) rather darker coloured than in ordinary cases of active inflammation.

Emetics and evacuants from the stomach and bowels are generally prescribed after the question of the propriety of blood-letting has been decided.

From what has been said on the subject of attempting to interrupt or arrest Typhous Fever, it will be readily understood, that I do not deem it necessary in every case to give either emetics or cathartics; but as these remedies are often necessary, it is important that we should point out, if possible, the circumstances which demand their use.

In cases of simple mild Typhus, where there is no nausea at the stomach, no pain in that region, where the heat is moderate, and

the pulse not greatly altered in frequency, I am clearly of opinion that we had better leave the disease to cure itself, as remedies, especially powerful ones, are more likely to do harm than good. In such cases, the patient gets along better without medicine than with; all that is required is to give him simple diluent (p. 57) drinks, a very small quantity of farinaceous food, and avoid as much as possible all causes of irritation.

The symptoms, which require the use of emetics, are nausea, sickness, and oppression at the stomach; and when required, it may be an important question what kind of emetic should be given.

The tartrate of antimony is an old remedy in the commencement of fevers, and when active inflammation exists, there is no one with which we are acquainted, that possesses so powerful an effect in suppressing it.

As some consider Typhous Fever a local inflammation, or an affection of the circulatory system dependant upon it, preparations of antimony would not seem inappropriate remedies. I will not take upon me to say that this fever is never connected with local inflammation, but if so, it is not with that kind which we generally denominate phlegmonic, or that, which tends to suppuration, nor that, which has been called sthenic, as is conclusively proved by the effects produced upon it by blood-letting, since this evacuation possesses (p. 58) a controlling influence over the one, while it has but a slight power over the other.

Though it may in certain cases obviate some of the troublesome symptoms of Typhus, and perhaps render the disease safer, yet it does not cure it, and in many cases is highly improper. So likewise, as far as I have been able to judge, tartar emetic should not be used in this affection, even at its commencement, and in the latter stages of the disease, it is sometimes followed by fatal consequences.

From the bad effects, which I have seen result from the use of antimony in this complaint, I have long since neglected it in my practice, and have substituted for it the ipecacuan, eupatorium, or the sulphate of zinc.

The use of this sort of medicines has generally been confined to

the commencement of the disease, but they are frequently proper and useful in its later stages. The articles, which I have just mentioned, either simple or combined, may be given, with safety and often with advantage, at any period when the symptoms are such as to demand an emetic.

(p. 59) Cathartics are recommended in almost all febrile diseases, and in many cases, much dependance is deservedly placed upon them; their general use, however, should not be indiscriminately recommended. In this, as in similar cases, we should consider the necessity of their administration, and whether they would probably produce the desired effect, not neglecting the particular means to be employed, and the extent to which we consider ourselves justifiable in carrying those means.

There are no remedies capable of doing much good, which under certain circumstances and in certain doses may not do harm, and I am persuaded that powerful ones of this class are always injurious.

Costiveness often occurs in the commencement of this disease. This kind of costiveness, is however, of a very different character from that which is habitual with some individuals, and which we so often meet with in stomach and bowel complaints, where the stools are unfrequent and the faeces hard and indurated.

(p. 60) The stools in this disease, except at its commencement, when there is generally an accumulation in the great intestines, are always liquid and possess a peculiar colour and odour.

The costiveness, therefore, consists only in the unfrequency of the discharges, and not in their consistence.

If a strong drastic cathartic be administered, it is often followed by a diarrhoea, which, though not always injurious when moderate, is always liable to become so.

I have never known a patient die of Typhus whose bowels were slow and required laxatives to move them, during the course of the disease. Laxatives therefore and not purges are required in this affection; and the milder they are, if they have the effect to excite the bowels to throw off their contents, the better, and even these should not be used too freely. If the bowels are shut up too long, their contents become offensive to the intestines, stimulate

them violently and a diarrhoea is more likely to follow, than if the bowels had been excited by a gentle laxative.

(p. 61) Laying aside the strong purgative drugs, we have a considerable number of mild cathartic ones to select from; epsom salts with senna, rhubarb, alone or with a very small quantity of calomel or ipecacuan given in small and repeated doses, are amongst the best articles of this kind.

Blisters have long been employed in fevers under the general impression that they were useful, without any very definite notion of the mode by which they produce a good effect, and without waiting for any particular symptoms indicating their use.

So far as my experience extends, they do not produce any very considerable influence on the disease; like bleeding, they will sometimes relieve local pains, when applied near the part affected, as on the forehead or back of the neck when there is pain in the head—on the breast, when the chest is affected.

In most cases if they do no good, they produce no bad effect; but when there are petechiae, or a disposition to haemorrhage, indicating great debility in the system of capillary vessels, they are liable to do harm, for in such (p. 62) cases, the blistered surface often becomes black and gangrenous.

Upon the whole, we cannot consider blisters as possessing much influence in Typhous Fever, and they may in most cases be dispensed with.

With regard to the perspiration, there can be no doubt, but that a great quantity of aqueous fluid escapes from the body in the form of vapour in Typhous Fever; but it does not become so condensed, during the hot stage, as to show itself in the form of a liquid on the skin, till there is some abatement of heat on the surface.

As there is more or less of sweating in the decline of most febrile diseases, and as a general perspiration is often accompanied with other symptoms of amendment, it has been looked upon as the natural cure of the disease. Upon this impression, it has been a pretty universal practice to encourage sweating; but with respect to the grounds upon which this practice is founded, it is a question, whether the effect has not, in this case, been mistaken for the

cause; that is, whether the (p. 63) sweating is not the effect of the amendment, rather than the cause of it; and if so, it is still more questionable, whether sweating, produced by art in the beginning of the disease, would be attended with good effects.

In all cases, where I have seen this sweating regimen adopted, especially when much external heat has been applied, the practice has been obviously injurious.

There are some medicines in the class of diaphoretics, which may be given with impunity, such as the ipecacuan, contrayerva, and the Virginian and Seneca snake roots, though they seldom or ever produce any sensible perspiration till the disease has formed a crisis, and then the patient will perspire freely without their assistance. When stimulating remedies are given internally and heat applied externally, to force a sweat, as it is called, the consequences are always bad at any period of the disease.

Opium in some form or other is often used in Typhus, and in many instances and under certain circumstances, may be useful, but is by no means an universal remedy, nor can it (p. 64) be administered with impunity in every stage of the disease.

When the patient is hot and suffers from pain in the head, and throbbing of the temporal arteries accompanied with confusion of mind, opium is generally hurtful and seems to augment rather than diminish these troublesome symptoms. But after their violence is in some degree abated, and the heat has become moderate, it may be used, and when combined with ipecacuan, sometimes gives rest and quietness during the night; although in many cases it will have the opposite effect; and serve to make the patient more watchful and restless. Under such circumstances, if persisted in, it does harm.

When diarrhoea occurs, opium combined with ipecacuan and camphor, is generally useful; and if it does not succeed in checking the discharge, does not appear to produce an injurious effect.

The use of this drug has also been advised in cases of great prostration of strength, that is, in cases where the morbid action is kept up in kind but has abated in force, owing to (p. 65) the exhaustion of the sensibility and irritability of the capillaries. In cases of this description it has been prescribed as a stimulus to



support the patient, and in such instances it must be acknowledged, that it is sometimes used with apparent advantage. But under the same circumstances, it does not always agree with the patient; and sometimes instead of quieting and giving him ease, produces a contrary effect, rendering him restless and watchful, and not unfrequently brings on or increases delirium, especially if given in large doses.

Upon the whole, opium may be used to advantage under certain circumstances in Typhous Fever, but cannot be considered as a specific in any stage, and is at best but a doubtful remedy.

A few years since mercury was, by many physicians in this country, considered a specific in Typhus, and its influence over the disease explained upon the principle that two kinds of morbid action could not exist in the system at one and the same time, and it was supposed that giving mercury so as to excite (p. 66) its specific action on the mouth, was substituting the mercurial disease, which was of short duration and safe, for the more dangerous febrile disease called Typhus. This ingenious explanation appeared very well in theory; all that seemed necessary was, that the facts should be found corresponding. Had this desirable incident happened, we should have possessed a very easy and safe mode of curing this somewhat intractable disease, by simply putting our patient under a regular course of mercurial remedies so as to affect his mouth for a reasonable length of time. But unfortunately, we have as yet discovered no such sure and easy method of curing Typhous Fever.

It was always acknowledged by the advocates for this practice, that in some and very severe cases, and those in which medical aid was most necessary, the mercury would not have its usual effect, and ptyalism could not be produced, and it was further confessed that in such cases if the mercury was pushed to any considerable extent, it produced a (p. 67) very bad state of the mouth, occasionally terminating in gangrene of the gums.

I have had several cases of necrosis of the under jaw, where I was compelled to remove a considerable portion of that bone, which had died evidently in consequence of an inordinate use of mercury during this fever.

In other cases, where calomel has been used early in the disease, and the mouth has been as favourably affected as could be wished, the disease nevertheless has run on forty or fifty days, and sometimes terminated fatally at a very advanced period. In some instances, after the mercury has affected the mouth, there has been a copious discharge of tough, ropy mucus from this part, which has been kept up for a long time after the other specific effects of the remedy had ceased.

This vitiated discharge of saliva is often accompanied with a vitiated secretion of the gastric fluid, and attended with a total want of appetite, and a constant ejection of every thing taken into the stomach.

Such patients have frequently recovered with difficulty, eight or ten weeks after the (p. 68) commencement of the disease. I have been consulted in many cases of this description.

Upon the whole, mercury cannot be considered a specific in Typhus, but may be an useful auxiliary in certain cases, that is, the blue pill or a small portion of calomel, combined with some other medicine, may be used with advantage. A small quantity of calomel with opium has in some cases checked a colliquative diarrhoea; and a grain of the same, joined to five or six of rhubarb, has done very well as a laxative.

Those physicians who consider Typhus as a disease arising from debility, have highly extolled the virtues of the Peruvian bark, and some have employed it through the whole course of the disease, while others have restricted its use to its later stage.

It is not from ingenious reasoning or fine spun theories, that we should estimate the value of a remedy, but from the effects actually produced by it in the majority of cases. Judging in this way, this remedy cannot be allowed a very high place, since as was before observed, the physicians just mentioned, (p. 69) who treat this disease with tonics and stimulants, have not been remarkable for their success.

I have prescribed the cinchona in many cases, and as far as I am able to judge, when there was a considerable heat present and while the mouth was inclined to be parched and dry, and especially when there was pain in the head, its use was injurious.

But in some cases, when there was a sense of coldness creeping over the patient and where there was hæmorrhage, it produced a good effect.

Upon the whole, the bark like mercury may be an auxiliary but cannot be considered an important remedy, much less a specific.

Bitter infusions may be used through the whole course of the disease, such as the eupatorium, (perfoliatum,) chamomile, and various others. When taken in considerable quantities, though they do not cure the disease, they may assist in preserving the tone of the stomach in some degree, and in that way aid in conducting it to a favourable termination.

(p. 70) Some twenty-five years since, the alkalies were proposed as remedies in febrile diseases, and for a time were considerably used.

They were introduced on the supposition that they possessed antiseptic properties, but they have not fulfilled the expectations of those who introduced them; nevertheless, I have occasionally seen them produce a good effect. Fever does not prevent the fluids from becoming acid in the stomach, and where this happens the moderate use of the carbonate of soda or of potash removes the irritation and burning sensation in the stomach caused by the acid; and thus far they may serve as palliatives, but I could never perceive that they possessed any other power over this disease.

The alkaline carbonates given with some acid, so as to evolve carbonic acid gas in the stomach, are generally grateful to the patient, and perhaps sometimes useful.

Those physicians, who adopted the notion that alkalies were antiseptic, of course considered acids as septic, and proscribed their use; and there were not wanting instances of (p. 71) their disagreeing with the stomach, especially the vegetable acids.

We have already mentioned, that fever did not prevent the fluids from becoming acid in the stomach, and I have, in several cases, witnessed a sensation of burning accompanied with an indescribable feeling of distress in that organ coming on after taking lemonade and other vegetable acids; but such cases are rare. In most instances, the vegetable acids, diluted with water, will be found grateful to the patient, and may, in almost all cases, be taken with impunity.

The mineral acids have been used as remedies in Typhous Fever, especially the muriatic and sulphuric. I have oftener prescribed the former than any of the others belonging to this class, and have thought the moderate use of it aided in preserving the powers of the stomach; but it is not a medicine upon which much dependence can be placed.

We were formerly taught to place some reliance on that class of medicines called refrigerants, viz, the acids and neutral salts. We have already had occasion to mention the (p. 72) acids, their refrigerating power is very trifling. As for the neutral salts, some of them may be used as cathartics in the early stage of the disease, when the heat of the body is considerable. The sulphate of magnesia, and the tartrate of potash are the best; but in the advanced stage of the disease, they sometimes produce an injurious effect on the stomach, and are apt to induce diarrhoea; this is more particularly the case with the sulphate of soda.

Nitre, or the nitrate of potash, was formerly a favourite prescription in fevers of all kinds. When this article is given in very small doses, it produces no perceptible effect, and if given in large, it does a positive injury to the stomach.

All things considered, we can place no dependence on internal refrigerants, and if we wish to produce this effect, that is, if we desire to diminish the temperature of the body, when above the ordinary standard, we must have recourse to cold water or cold air.

The heat may be lessened by covering the patient lightly, and admitting cool air into the (p. 73) room, when the season of the year will admit of it, or by admitting the air in contact with the skin, by raising the bedclothes on one side of the bed, and bringing them down suddenly again; in this way we can cause a current of cool air to pass over the body, which will conduct off the heat and greatly refresh the patient.

But the most effectual method of reducing the temperature of the body is by the use of cold water, which may be taken internally, or applied externally. When persons, sick of this disease, desire cold water to drink, it should never be denied them—they should be allowed to drink *ad libitum*. The quantity of heat abstracted from the body by the water which they will drink, however, is but small, and except in cases where, by its influence

on the stomach, it produces perspiration, its effects are very trifling.

The only effectual method of cooling the body, in these cases, is by the use of cold water applied externally; by this means we can lessen the heat to any degree we please. Different physicians have adopted different (p. 74) modes of making the application. Some advise to take a patient out of bed, pour buckets of water upon him and then replace him again; while others prefer sponging him with cold water. We have cases, where cold water would be of service, in which our patients are too much reduced to be taken out of bed and placed in a sitting posture without injury. In these cases a different management will be necessary. The method, which I have adopted, is to turn down the bedclothes and to dash from a pint to a gallon of cold water on the patient's head, face and body, so as to wet both the bed and body linen thoroughly. It is better that he should lay on a straw bed when this is done, it is not however essential. If his body should be very hot, he may be turned upon his side, and the water dashed upon his back.

As soon as his linen and the bedclothes begin to dry, and the heat in the head and breast begins to return to the surface, the water should be again applied, and in this way the heat may be kept down to the natural standard or rather below; on the surface, so that (p. 75) the skin may feel rather cool to the hand of a healthy person.

It is not very material what the temperature of the water is, if it is below blood heat, excepting the shock given by its first contact, which in cases where there is much stupor or coma, is of some importance; in general, the effect is produced chiefly by the evaporation.

All additions made to water used for this purpose, such as vinegar, spirits, &c. are injurious. The former, on being evaporated on the surface of the body, covers it with a thin pellicle formed by the sediment, which makes the skin feel stiff and unpleasant, and spirits evaporated about a sick person produce an offensive odour and likewise leave some impurities on the skin and clothes.

When water is used to wash the body, as is often necessary in this fever, soap, or the carbonate of potash may be added, but when used to reduce the heat alone, pure water will be found best.

When the temperature of the body is such, that it does not require the general application (p. 76) of cold water, still it may be occasionally applied with advantage to the head and face.

Whenever there is any dryness of the lips, teeth or tongue, it may be relieved by letting water, slowly squeezed from a sponge or cloth, fall on the mouth and over the whole face; this should be repeated often enough to keep the mouth clean and moist.

I have produced a good effect by laying a piece of thin loose muslin over the face, so as to have the air drawn through it in the act of inspiration, at the same time keeping it constantly wet with cold water; in this way, the vapour inhaled into the lungs, proves very grateful to the patient.

I could state many cases in which cold water was applied with the most unequivocal advantage.

In the summer of 1798, the first year in which this fever occurred in my practice, T. B., a young man of about twenty-five years of age, was brought into my neighbourhood sick of Typhus, for which he had been bled before I saw him; the fever was severe, and his unfavourable symptoms increased for several days. (p. 77) In a consultation, it was agreed to put him into a warm bath, which was done.

He was a little delirious before he went into the bath, and when he came out, was raving. From this state, he sunk, in the course of the next night, into a low muttering delirium, with a great degree of coma and starting of the tendons, and with scarcely the ability to swallow. His pulse was irregular, but still possessed some force, and his heat was above natural. Twenty-four hours were passed in this situation, without any symptoms of amendment. The next day when I visited him about nine o'clock in the morning, the weather being very warm, (as it was in the month of July,) a young man, who had engaged to attend him that day, came in, bringing a gallon pitcher full of cold water, which he had just drawn. Finding the patient's pulse had some strength and his heat continued above natural, I stripped him

naked as he lay on a straw mattress, and poured the gallon of water over him from head to foot. He seemed to feel the shock, but did not speak. The young man in attendance was ordered to repeat the affusion as (p. 78) often as he began to grow dry and warm, which was punctually performed.

When I visited him a little after sunset, his heat was diminished and his pulse did not intermit as often as it had done. He was then taken off the wet bed and laid on a dry one, likewise of straw, with nothing but a linen sheet spread over him, the windows of the chamber were kept open through the night and a dose of opium and musk was prescribed and taken. No other internal remedies were administered. The next morning there was no alteration. The affusion of cold water was renewed as the day grew warm and the heat was kept down through the day as it was the preceding one. Before night, the patient recovered so as to speak, called for more water, and said he wished to be put into the river. From this period he became convalescent, and recovered without the use of any other remedy.

In the month of September, of the year 1800, I visited A.P. a strong robust man, aged between thirty and forty years. He had been sick about a fortnight, his head was not much (p. 79) affected but the heat was great and his thirst urgent. My visit was in the evening. The body was stripped, that is, the sheet which was thrown over him was removed, and his shirt divided down before so as to expose his body, and about a quart of cold water was applied by sprinkling it on with the hand. The sheet was then thrown over him; and the water applied as often as he became dry and the heat began to return. A little peruvian bark, mixed with some nitrate of potash, was all the medicine taken. Previous to this he had drank, every night, two quarts of some diluent drink, for several nights in succession. After the first application of the water, that parched sensation of the lips and mouth, which urged him to drink so much, abated, and he lay the whole night without any desire to drink. The next day he was convalescent, and recovered without medicine.

I. B. a strong robust man, aged between thirty and forty, had

been sick a fortnight when I first visited him; his pulse was frequent, his heat great, and his mouth exceedingly parched, so much so that he could not sleep but for (p. 80) a very few minutes at a time without being awakened by a sense of thirst. His feet were very cold.

This individual had been badly treated, and his friends had been prevented from changing his linen and bedclothes by the physician, who had fears that he would take cold!

The patient was first shaved, an operation which had not been performed for something like a fortnight, he was then slipped down in the bed so as to drop his feet into a vessel of warm water and soap, where they were rubbed till they became clean and warm. The bed and body linen were then changed and he was properly placed in bed. The affusion of cold water was commenced over the head and breast, and repeated sufficiently often to keep down the heat. The distressing thirst was removed at once, he became convalescent the next day, and recovered without any further medical treatment.

I could detail a great many additional cases, where the good effects of cold water were as apparent and as immediate as in the cases just cited; and in no instance where I have used (p. 81) it, or seen it used by others, has it done harm. There are cases, however, where its application is not called for; at the same time there are but few in which it may not in some stage of the disease do good. It is always grateful when applied to the face and mouth, and its vapour is very salutary and refreshing to persons sick with fever.

It will be observed, that the first time I used cold water externally in fever, was in 1798, the first hint of which I took from Dr. Robert Jackson's work on the Fevers of warm climates.

With regard to diet, it is not necessary to say much; if patients were left to select for themselves, without the interference of nurses and friends, who are always afraid they will starve, they would generally decide right, since they would not often take anything, that could be called food. The farinaceous and mucic-



luginous substances are the only articles of nutriment admissible, with the exception, perhaps, of milk largely diluted with water, or whey prepared from it.

(p. 82) All solid food is injurious, and all sorts of broths prepared from animal substances should be prohibited.

After the fever has formed a crisis, and the secretions of the mouth have become healthy, the appetite generally returns, and if we then allow the patient to choose for himself what he will eat, and take care that the quantity taken at first is very small, he will not often be injured by it. But it is not safe to let patients judge as to the quantity. Their minds are weak, and their appetites strong, and they would, if allowed, often hurt themselves by too much indulgence.

With respect to liquids, I have generally let the patient choose for himself, provided he does not select any of the stimulants, such as ardent spirits or strong beer, which, however, is almost never the case. Cold water, or water acidulated with one of the vegetable acids, small beer or brisk cider are the drinks which are usually preferred. The infusion of the pleasant aromatic herbs may be always allowed.

(p. 83) Besides giving directions for the use of medicines, it is important that we should direct, what may be called the general management of the patient.

When an individual is first taken sick with Typhous Fever, we should expect a disease of considerable length, and make our arrangements accordingly. If the thing is practicable, he should be kept in a spacious room, the larger the better. His bed should be of straw or husks, especially if it is in the warm season; and it should not be placed in the corner, but brought out into the room. We should contrive to have a current of air pass over the bed by means of doors and windows. It is well to have a chimney and fireplace in the room, and in the night when the air is very still, (though the weather should be warm,) a small fire kindled with a little dry wood, so as to cause a current of air up chimney, and by that means often change the atmosphere of the room, will be found of service. In the warm season of the year, the windows should be kept open night and day. All the furniture (p. 84)

should be removed, except such articles as are required for the patient's use. The windows should be darkened, or something opposed to the light, in such a way as to still admit the air. The room should be kept as quiet as possible, since noise is injurious, and no more persons should be admitted than are necessary to take care of the patient, which will, if he is very sick, require the labour of more than one.

The room should not be carpeted, and the floor should be often washed with pure water, or soap and water, and in the hot season, it, as well as the walls, may be kept wet with water during the heat of the day.

Cleanliness is absolutely essential to the patient's comfort, and no dirty dishes or useless medicines or food should be suffered to remain in the room. All excrementitious matters should be removed immediately. In the warm season, of the year, the bed and body linen should be changed every day, and in the cold, every other day at farthest.

The patient's body and limbs should be (p. 85) cleansed every day with a piece of sponge and warm water or soap and water. If a male, he should be shaved every day or every alternate day, and if a female with long thick hair, it should be cut off or thinned, so as to leave but little of it the full length.

THE END



## Observations on the Pathology and Treatment of Necrosis\*

BY

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**T**HE etymological definition of Necrosis is, the *death* of some part of the bony structure. As technically employed in medicine and surgery, however, it designates a particular form of disease, characterized by peculiar symptoms, and often, generally indeed, terminating in the death of a portion of the bone in which it is located. We may perhaps question the propriety of the above appellation, if it be made to appear, as I shall attempt, that the death of the part affected is not the *necessary* sequel of the disease, although the most frequent. It is the same inconsistency of language that obtains in the application of the term hydrocephalus to those inflammatory affections of the meninges of the brain, which sometimes terminate in dropsy of that organ.

This disease was formerly known in New England under the name of *fever-sore*, given to it, undoubtedly, because it is generally accompanied, from the very commencement, (p. 98) with a high degree of constitutional irritation and symptomatic fever. The constitutional disturbance, in most cases, being nearly synchronous with the local affection, induced medical men, while the humoral pathology prevailed, to regard the general disease as a fever, and the local affection as nature's remedy, by which she

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eliminated the peccant humours.—They probably would have explained it in the following manner:—The fever, to expel the morbid matter from the system, throws it on the part affected, which causes the inflammation and subsequent collection of matters.

The following pathological history of this disease has been the result of extensive observation, the disease very frequently occurring within the sphere of my practice.

Necrosis commences with an acute inflammation, either in the bone itself or its investing membrane, accompanied with an acute pain, not always at first in the part affected, but often felt most severely in the joint nearest the disease. In a day or two, however, it generally leaves the joint, and permanently locates itself in the part inflamed.

Almost from the first commencement of the pain there occurs severe symptomatic fever of the inflammatory character. The local affection generally terminates in suppuration, frequently as soon as the fourth or fifth day, and this event, if it occur, is rarely protracted beyond the tenth or twelfth. The matter is at first deposited between the external periosteum and the bone. When the shafts of the long bones are the seats of disease, about the same time that matter is deposited beneath the external periosteum, there is formed a corresponding (p. 99) collection between the internal surface of the bone and the membrane surrounding the medullary substance, so that there then exist two collections of matter bathing the opposite sides of the walls of the bone. This fact, which I deem of great importance, as being essential to the correct treatment of the disease, I have ascertained in repeated instances, by the operation which I have performed for its relief, namely, the trepanning of the bone.

Very soon after the attack, the whole limb swells, but there is no marked tumefaction immediately in the part affected, till after the matter makes its escape from the periosteum, and is diffused beneath the adjacent soft parts. Whenever this occurs, the extreme pain and symptomatic fever, which till then have continued unabated, in some degree subside, but do not entirely leave the patient.

When this kind of inflammation attacks the spongy bones, the matter is at first collected on both sides of the external lamella, or plate of compact bone, which covers the cells, so that it is similar to the same disease in the long bones, except that in the latter the matter within the bone is lodged between the medullary substance and the walls of the bone, the medullary substance not being affected nor penetrated by the matter.

The death of a portion of bone, in this disease, does not appear to arise from any extraordinary malignity in the inflammation, nor from its exerting any peculiar lethiferous influence upon the part affected, as some specific diseases destroy the parts which they attack.—Abundant cause for the death of the part is found in the insulation of the bone, effected by the accumulation of (p. 100) matter on both sides of its parietes, and the consequent destruction of those vessels which, from the two periosteæ, furnish it with blood and nutrition, so that the denuded portion receive no vessels but those extremely attenuated ones, which permeate it from the surrounding margin of healthy bone. These last being insufficient for its nutrition, it consequently perishes. Nature then sets up a process of ulceration for the separation of the dead portion, and the evacuation of the matter contained within it, this occupying a greater or less time, as influenced by circumstances. The dead and insulated bone, from its indestructible nature, remains as a foreign body in the living parts, until, by the recuperative efforts of nature, it is dislodged entire and rejected from the system; or, being constantly bathed in the secretions which protect the surrounding parts from its contact, is gradually dissolved and wasted away; or, finally, is removed by art.

When the disease has arrived at that period at which the matter accumulated beneath the periosteum has made its way to the surface, and that contained within the cavity of the bone has issued through a fissure in the same, relieving the parts from the irritation of distension and pressure, the symptomatic fever in a great degree ceases. If, however, the collection has been large, and the portion of necrosed bone be considerable, hectic fever is

liable to supervene, indicating the continuance, though a change of irritation.

Whenever there occurs a favourable respite, the conservative powers of nature, always active so long as vitality remains, rally for the purpose of remedying the injury inflicted upon the bone. The process instituted (p. 101) for this purpose varies according to circumstances.—When the portion of dead bone, is small and situated on the side of one of the long bones, granulation will shoot from the surface of the sound or living bone, and as occurs in mortification of the soft parts, will push the dead bone off from the living, and finally urge it through the opening previously formed, and disengage it from the body. This is more likely to happen when the soft parts have been divided early in the disease, over the whole length of the dead portion of the bone.

But in those cases in which a large portion of the circumference of the bone is affected, and especially when the life of the whole circumference, to some extent, has been destroyed, there is formed a bony structure, which attaches itself to the healthy bone, near, or at the part where it has separated from the sequestra or dead portion, around which it forms a bony case, complete, excepting the apertures through which matter flows, and which must thus remain open. The new cylinder of bone does not closely embrace the dead; hence, and also because it overlaps the ends of the living bone, it is to the feel considerably larger than the bone of the sound limb.

Necrosis is almost exclusively confined to young subjects. I have very rarely seen it in persons under five, or over twenty-two. I have, indeed, witnessed a disease in old men which might perhaps be denominated necrosis, as terminating in death of the bone, but characterized by very different symptoms. Three cases have fallen under my observation, in each of which the upper part of the femur was the part affected. Two of the patients were over seventy, the other much younger, (p. 102) but with a broken constitution, having some years before lost the prepuce and glans penis by a gangrenous inflammation. The disease attacked with considerable pain and constitutional affection; there was, how-

ever, for some days, no swelling nor appearance of inflammation externally; but at length the limb became tumid, and a fluctuation was perceived. On opening the part, a considerable quantity of dark and very offensive sanies was discharged; the bone appeared denuded of its periosteum, and of a dark colour. These cases all proved fatal in a short time. In one, the affected portion of bone was separated before the patient died.

In regard to the locality of necrosis, although, perhaps, every portion of the bony fabric is liable to its attacks, yet it occurs in some bones much more frequent than in others.

I have never seen it in the scapula, sternum, nor spine. It very rarely occurs in the bones of the carpus, although I have occasionally seen it attack the fingers. The bones of the cranium are not exempt from it, and it often attacks the lower jaw, the clavicle, and the ribs, but especially the long bones of the arm, fore-arm, thigh and leg. I have seen it in the femur, patella, both bones of the leg, os calcis, metatarsal bones and the bones of the great toe.

My own experience would determine the tibia to be the most frequent seat of the disease, next to this, the femur, and then the humerus.

I am induced to believe, that this kind of inflammation never attacks the articulations in the first instance, but, in the long bones, is confined to their shafts, and when it attacks the spongy bones, as the os calcis, it (p. 103) does not commence in the articular surfaces, nor within the capsular ligaments. The joints are, indeed, sometimes affected by this disease, but, when this does occur, it is the result of disease extended from the shaft of the bone. The margin of the sequestra is often accurately defined by the line of junction between the shaft and epiphysis of the bone, the articular portion being thus left untouched. It sometimes happens, however, that when the attack is in one of the larger bones of the limbs, and near to the apparatus of the joint, the inflammation extends to the latter, matter is formed within the capsular ligament, and the limb is lost. Such cases, however, are exceedingly rare; in the whole course of my practice I have had occasion to amputate but two limbs, for the purpose of rescuing the patient from this formidable variety of the disease.

Necrosis is not always confined, in an individual case, to one bone, but may occur simultaneously in remote parts, or, which is more common, successively. The secondary attack is not so often on a bone of the same limb as on one of another. When the first attack has occurred in the femur, the second has located itself in the humerus, and vice versa. In a few instances, however, I have observed it in a bone of the same member, attacking, for instance, the femur and the tibia successively. In a few instances it has attacked secondarily the same bone in the opposite limb. I once saw a patient who had had, in the course of a few years, an attack of this disease in almost every bone in his body.

In regard to the general prognosis of the disease, I have observed that a very great majority of patients survive its attack, though often with long confinement, (p. 104) protracted suffering, and great emaciation. In a few cases, however, the disease proves fatal, and when it does so, it frequently happens at an early period of its progress, and life is destroyed by the extreme degree of constitutional irritation and symptomatic fever. These fatal symptoms are especially apt to occur when the disease occupies a considerable portion of a large bone.—This severity of the constitutional symptoms probably depends on the peculiar structure and sensibility of the part particularly affected. The periosteum, beneath which the matter first accumulates, being a fibrous membrane, possesses, indeed, but very little sensibility in health, but when inflamed, especially when put upon the stretch by distension, it is known to be the seat of the keenest sensations, and to be a source of extreme general irritation, giving a greater shock to the nervous system, than almost any other diseased structure.

In some cases, in which the disease has destroyed the vitality of a large portion of one of the long bones, and in which there must necessarily have occurred extensive suppuration and copious discharge of pus, the patient, as in similar results of other diseases, has died of exhaustion.

The patient, also, after having survived one or two severe attacks, sometimes is cut off by the accession of another, and



when this is the case, death generally occurs in the stage of excitement and constitutional disturbance.

**DIAGNOSTIC SYMPTOMS OF NECROSIS.**—It is impossible, even by the most vivid description, to express the character of this disease with the precision with which the observation of a few cases will convey it; and yet, before (p. 105) one can observe with accuracy or profit, he must know something of its history.

At the disease is an acute inflammation, characterized by the peculiar vital properties of the parts affected, many of the symptoms must be analogous to those of other inflammatory affections. I have often known it to be mistaken, and for a considerable time treated, for acute rheumatism, even although suppuration may have been observed.

In my pathological observations on the disease in question, I stated that it commenced with acute pain in, or near, the part affected. It frequently happens that, when the disease fixes on one of the long bones and near its extremity, the pain is complained of in the adjacent joint; thus, when the disease attacks the lower portion of the tibia, the pain is for a time chiefly felt in the ankle. If in the upper part of the tibia, or lower part of the femur, it is referred to the knee joint. It is not long, however, confined to the joint, but fixes itself in the inflamed part. It is this circumstance of pain, referred to the joint, that often causes the diseases to be denominated rheumatism.

The pain experienced in necrosis is extremely acute, unremitting, and not much influenced by the motions nor position of the limb. The pain is often a day or two antecedent to the swelling, and when the latter first occurs, it is generally diffused over a considerable part of the limb, especially below the part affected. —The surface is rather firm to the touch, but the skin is not discoloured till after matter is formed and advanced towards the surface. The symptomatic fever is coeval with the pain, they both usually occurring on the same (p. 106) day. The pulse is both frequent and quick, the stroke sudden, and the artery small and hard to the touch. At first the patient has occasional chills, but when he complains of a sensation of cold, the skin, to another person feels hot. The pain is so tormenting, that he gets but

little or no sleep, during the night is often delirious, though during the day rational. The tongue is furred with a soft, white coat. The face is not flushed, but rather pale; with the exception of occasional red spots on the cheeks. The hands are often hotter than other parts of the body, and in one violent case I observed that the points of all the fingers were red, swollen, hot and very painful. The appetite for food is lost; thirst considerable, but the stomach and bowels are not so much affected as they generally are in other febrile affections.

It has already been stated, that the disease is acute, and that suppuration takes place promptly, but there is often a difference of several days in different cases, though this difference is often more apparent than real. But few surgeons have the tact to discover matter while it is confined beneath the periosteum, and more especially where the part is covered by voluminous muscles, as is the case in the thigh. In this instance it is probable that an experienced surgeon might not be able to detect the presence of pus, till after it had made its escape through the periosteum, and accumulated to some extent in the soft parts.

I have observed that the locality of the pain, in the early stage of the disease, caused necrosis to be sometimes confounded with rheumatism. Most, even of its early symptoms, however, are very different from those (p. 107) of that disease. The symptomatic fever and constitutional irritation come on sooner after the local attack, and are much more severe. The pulse, as described above, is also very different from that of acute rheumatism, it being smaller, harder, and less easily compressed. Suppuration, which very rarely occurs in rheumatism, finally removes all ambiguity. Necrosis, also, usually attacks at that period of life when rheumatism is not so liable to occur.

The fever attending necrosis is distinguishable from typhus by the local affection, by the pulse, which is harder and less easily compressed, and by its not being attended with so much stupor. The stomach and bowels are also much less affected; besides, there is the different expression of countenance, which is very apparent and characteristic to the eye, but is not easily described.

CAUSES OF NECROSIS.—The inflammation which produces nec-

rosis of the bones, has sometimes been excited by blows and injuries inflicted upon the limbs. The sudden suppression of perspiration, by application of cold to the surface, has the same relation to this disease as to many others. In several cases I have known it to occur immediately after the patient had imprudently bathed in cool water, when the surface of the body was warm. It often, however, seizes the patient without the intervention of any obvious exciting cause, by which the lurking diathesis is sometimes developed, or concentrated upon a particular part.

It is customary with physicians and surgeons to ascribe necrosis to a *scrofulous* diathesis as its predisposing cause. This term is employed with much latitude, (p. 108) and is often used, like the sign of an unknown quantity in algebra, to express something with the nature of which we are unacquainted. When used in this way, there is perhaps no impropriety in naming scrofula as the diathesis which predisposes to necrosis. Necrosis, however, is by no means to be identified in its nature with the affection of the lymphatic glands, to which the terms scrofula is, with more precision, applied, since necrosis may repeatedly occur in the same individual without being accompanied by lymphatic tumors. Whatever the remote cause may be, it is undoubtedly one which produces an enfeebled state of the capillary system, in consequence of which the nutrition of the bones, usually requiring the exercise of nature's powers in their integrity, is performed in an imperfect manner, and they become liable to the encroachments of disease.

TREATMENT.—I have already, I believe, hinted that it very rarely happens that this kind of inflammation terminates by resolution under the ordinary treatment. Though I have seen a very great number of cases of necrosis in their progress, yet the number of cases which have fallen under my care, in the first instance, has been small; almost all the cases of which I have had the management have been under treatment for a longer or shorter time before I have been consulted; so that I have drawn my inferences as to the effects of the different modes of treatment

employed in this stage from what I have known to have been done by others, rather than from what I have myself done.

The treatment first resorted to has been, in some cases, bleeding; and in all, cathartics. Sometimes (p. 109) emetics have been tried. The topical applications have been blisters, evaporating lotions, and cataplasms. In some cases all these remedies have been employed before I have seen the patient. But I do not recollect a single case in which I had reason to believe that the inflammation was seated in, or on the bone, that has not terminated in suppuration. One I recollect, in which I saw the patient on the third day after the attack, when I bled as freely as I dared to do, and kept the part constantly covered with cloths, wet with cold water, besides giving cooling cathartics; but suppuration, nevertheless, took place.

The following case will serve to illustrate the pathology of the disease, and the mode of treatment which I shall recommend. It occurred in 1798. The patient, a colored girl, nine years old. The attack was on the femur, and had been of sometime standing before I saw it. There was a large collection of matter in the thigh, which extended from a small distance above the knee to near the trochanter. An incision was made on the outside of the thigh, commencing near the knee joint, and extending upwards eight inches in length.—A large quantity of matter was discharged, and on examining with the finger, the bone was found denuded of its periosteum, from two or three inches above the articulation of the knee, upwards, two-thirds of its length; and near the lower end the whole circumference of the bone was stripped of its periosteum, excepting the *linea aspera*; which formed a kind of septum between that part of the matter deposited on the inside of the bone, and that on the outside. But on the anterior surface of the bone there was a free communication, (p. 110) so that I could pass my finger over the bone, and turn it down to the *linea aspera*, where the muscles, tendons, &c. still adhered to the bone. At this time I had but little knowledge of the disease, and no book which I had seen rendered me much assistance. Benjamin Bell, in his *Treatise on Ulcers*, directs, in such cases, to perforate the bone down to the living parts, in order

to produce exfoliation. This I had tried in several cases, but with no good effect. In this case, as the bone, to some extent, was exposed to the sight, I concluded to wait a few days, and see if granulations would appear on the denuded bone.—But in a short time the bone which was exposed to the sight began to assume a darker colour. I then determined to remove a portion of it, in such a manner as to go through the dead part, let that be more or less.—For this purpose I used the round saw employed in operating on the skull, applying it to the outside of the femur, nearly in the centre of the denuded part, and sawed through the walls of the bone down to the medullary substance, and then removed the piece circumscribed by the saw, which exposed to view a portion of the medullary substance, in extent equal to the diameter of the saw.

On sponging out the blood, the medullary substance appeared healthy, and was firm to the touch, but on looking attentively at it, I perceived purulent matter issuing, by pulsations, from beneath the sawed edges of the bone, and between the bone and medullary substance. I repeatedly wiped it away, and it continued to gradually issue. The walls of the bone being fixed, the matter was not forced out by their collapse, as it is in the (p. III) soft parts; but as there is an increase in the quantity of blood in the medullary substance, at each systole of the arteries, this substance is enlarged, and of course the matter is pressed out.

After the operation of sawing the bone, the wound was treated with the simplest dressings. In a few days after this, the bone, which was of a pearly white, a little verging to brown, where exposed to the external air, changed its appearance, assuming a carmine colour, and finally recovered, with no other loss of substance than a thin scale, which separated from the surface of that portion which had been touched by the saw, the whole of which did not exceed ten grains.

This case established in my mind the pathology of the disease and the proper mode of treating it; that is, when the disease has advanced so far as to form matter. But it would be a desirable thing to prevent the formation of matter in such cases, if possible. I have already stated that, in the common mode of treatment,

this is rarely effected. I did not, however, intend to be understood that this is impossible, or that there is no other mode of treatment that might be adopted, which, if seasonably employed, might arrest the progress of the disease, prevent the collection of matter, and, of course, preserve the bone from injury, or the necessity of making a breach in the bony structure.

As the disease passes through several different stages, which require different modes of treatment, the practice must vary accordingly. If the surgeon has the good fortune to be called on the first attack of pain, supposing the disease to be in one of the long bones of the limbs, as soon as the disease, by swelling and tenderness (p. 112) of the part, has sufficiently marked the seat of the inflammation, an incision should be made, in a longitudinal direction, through all the soft parts down to the bone, and through the periosteum. The extent of the incision should be equal to the extent of the inflammation. Since I have adopted my present opinions of necrosis, I have not been fortunate enough to be called in till matter has been formed, and therefore have not had it in my power to test this mode of treatment, but have communicated my views on the subject to those who have had opportunities of applying them to practice, and in every case that I have heard of, the incision has arrested the further progress of the disease, and the case has been reduced to the state of a simple incised wound, which has soon healed, without any injury to the bone. This effects a very great saving of time, pain and confinement to the patient.

Necrosis, on the larger limb, is somewhat analogous to the felon on the finger, where the parts beneath the strong fascia of the part are inflamed. In both cases a fibrous membrane is concerned, and, as in felon, an incision carried through the fibrous membrane to the extent of the inflammation, stops the further progress of the disease—so, in necrosis, when the soft parts, with the periosteum, are divided, the disease is cured. After the incision, the treatment, both general and topical, should be such as we recommend in cases of simple incised wounds, attended with considerable inflammation; excepting that we should not try to approximate the edges of the incision by adhesive plaisters,

but dress them with simple applications, such as lint, spread with simple cerate, and evaporating lotions applied to a (p. 113) considerable portion of the limb, at least as far as the inflammation has extended. The general treatment consists in cooling purgatives, nauseating doses of antimony, and opium sufficient to allay irritation and procure rest.

When the disease happens to be seated on the spongy bones, as the os calcis, metatarsal bones, &c. the incision should be made in the direction of the muscles, tendons, arteries, &c. which may pass over it, so as to avoid wounding these organs. In other respects these cases are to be treated in a similar manner, as the above.

When the disease affects a bone thinly covered with soft parts, as the anterior part of the tibia, lower part of the fibula, or the humerus, clavicle, ribs, &c. surgeons at this day would not hesitate to make the proper incision. But when the femur is the bone affected it will be otherwise. The precise part affected is not so easily detected, and probably few practitioners would venture to make so bold an incision under such circumstances. But when the seat of the disease can be clearly ascertained, the propriety of making such an incision cannot be doubted; and when we consider that the pain and confinement consequent to an incised wound of almost any extent, is so trifling, compared with the evils attendant on a long-protracted case of necrosis in this bone, it should render us bold in directing the incision.

The second stage of this disease, when the matter has formed between the periosteum and the bone, still admits of a cure without any loss of bone. If, in this stage of the disease, an incision is made through the (p. 114) soft parts, and the periosteum be divided as far as it is separated from the bone, and a portion of the bone be cut out with a saw, or several perforations be made in the bone which has been denuded, down to the medullary substance, so as to allow the matter collected between that substance and the walls of the bone to escape, the necrosis or death of the bone will be prevented. By this mode of treatment I have succeeded perfectly in arresting the further progress of the disease in the bone, and the patient has recovered without loss of

any portion of it. If this mode of treatment be put in practice early enough, and the perforations be made in the bone sufficient to afford a free exit to the matter, it will always succeed. The best instrument for perforating the bone is a small trephine that cuts out a piece about the size of a nine-penny-bit; but I have often succeeded by making a number of perforations through the denuded portion of bone, with the perforator used in trepanning. When this instrument is used, there should be several perforations made, more or less, according to the extent of the denuded portion of bone, and the instrument should be carried a little into the medullary substance, otherwise the aperture will be too small to admit the matter to pass freely.—After this operation has been performed, the case is to be treated as we have directed, where the incision has been made before matter has been formed, that is, in the simplest manner.

In the third stage of this disease, the matter has made its escape through the periosteum, and obtained a lodgment in the soft parts, with more or less tumefaction of the part, and a perceptible fluctuation. The (p. 115) treatment, in this stage, is precisely the same as in the second stage, but the favourable result is not so certain, as a portion of the bone may have been deprived of its circulation too long, or may be perfectly dead, and the separation between the living and dead bone may have commenced. In that case, the operation cannot save the bone entire; a portion must necessarily be cast off. Nevertheless, the incision should be made through the whole length of the collection, taking care not to divide any important parts, such as tendons or large arteries. The bone should then be perforated and a portion sawed out, so as to give free vent to the matter contained within it, and the wound treated as after the operation performed during the two first stages.

I would advise a free incision, with a view to the subsequent treatment of the case; for if a large portion of bone should be detached, it affords a better opportunity for its removal.

As we cannot always be certain whether the bone may, or may not, be in a recoverable state, the operation, though late, may prevent the destruction of any portion of it, as I have several



times had an opportunity of witnessing, and when I had not expected such a result, on account of the length of time which had elapsed before it was performed. If a portion of bone should be cast off, the perforation will enable the operator, if it should require an operation for its removal, to break it the more easily, which is often a necessary part of the operation in removing a large sequestra.—The operation of sawing and perforating the bone gives no other pain to the patient than what arises from pressure of the instrument on the limb, which need (p. 116) not be considerable. After the operation has been performed, in either stage of the disease, nothing more need be attempted, and no instrument, not even a probe, should be thrust into the wound. If the collection of matter in the soft parts has been great, and the discharge continues to be copious, the patient should take bark freely, and should be supported by as nutritious a diet as the stomach will bear.

In some cases, in which the discharge has been very copious, I have checked it by throwing in a solution of corrosive sublimate, of the strength of ten grains to a pint of water, to be repeated once in four or five days, and when the matter has been very offensive, a weak solution of carbonate of potash, thrown into the sore with a syringe, from time to time, removes the offensive odour.

As it will often happen, either from nothing having been attempted to prevent the death of a portion of the bone, or from the necessary operation having been delayed too long, that a portion of the bone, of greater or less dimensions, loses its vitality, and becomes a foreign body, surrounded by the living parts. When this happens, if the portion of dead bone is of any considerable size, there will be a discharge of matter kept up as long as the sequestra remains.

The object of the surgeon, then, is to remove the sequestra. The first question is whether we shall attempt to remove the sequestra by an operation, or leave it to the unassisted efforts of nature, and the decision must be determined by contingent circumstances, like every thing relating to our art.

If the portion of dead bone is small, and but a (p. 117) trifling

discharge of matter be kept up by it;—and if it is so situated that it does not give much pain, nor impede the use of the limb,—and especially, if it is situated near the surface, it may be left to the operations of nature, till it appears to be coming away, when its removal may be facilitated with the fingers or forceps.

But where the portion of dead bone is large,—a considerable discharge kept up by it, and especially when it deprives the patient of the use of the limb, an operation, undertaken for the purpose of removing it, is generally to be preferred, and the first question to be settled in such a case, is, at what time shall the operation be performed?

When the disease has not extended over the whole circumference of the bone, that is, when only a portion of one side of the bone is affected, the dead portion may be removed, if the operation be thought necessary, at any time after the dead bone is detached, which is generally in no very great length of time. This can be ascertained by the sound it gives on rapping it with a probe, or any other instrument, and more certainly by pressing directly upon it with the end of the probe, for sometimes we can perceive that the sequestra is moved by the pressure. When this cannot be perceived, if, when you fix the end of the probe directly on the dead portion of bone, you make considerable pressure upon it, and the patient complains of pain, you may be certain that the bone is detached, as such pressure will otherwise cause no sensation, for they are granulations which have started from the edges of the living bone that are hurt by the pressure. In such cases the dead bone had better be removed early, otherwise a new bony (p. 118) structure will be formed over the sequestra, which may make it necessary to remove some portion of the former with the saw, which would be avoided by a timely operation.

But when the whole cylinder of the bone has been destroyed, that is, when the sequestra consists of the whole bone for a certain portion of its length, the operation must be deferred till the new bony structure has formed round the sequestra. This is necessary to preserve the length and shape of the limb, for if the operation should be performed before this process is perfected, the

member would be reduced to the state of a broken limb, with a deficiency of bone between the two ends of the living bone, and the limb would undoubtedly be shortened; and it is not quite certain that the bone would form in such a manner as to support the body.

It is not difficult to ascertain whether the new bone has formed round the sequestra or not. When this has taken place, there is considerable enlargement of the limb at that part of it, and it feels hard, as though the bone were much larger than natural, which is really the case, and if a probe is inserted into the opening through which the matter issues, the dead bone will be felt, and around the edges of such opening the new bone also, though not yet firm and solid, and the probe may often be inserted between the new bony covering and the dead bone. Under these circumstances, the sooner the operation is performed the better.

Respecting the operation, the cases which occur are so peculiar, and require such different methods, that nothing more than general directions can be given.—The object, however, in every case is the same; that (p. 119) is, to remove a piece of dead bone, which has become a foreign body as it relates to the living.

The instruments which may be wanted in this operation are a probe, knife, round saw, and one or more of Hey's saws, several pair of strong forceps, and a pair of cutting forceps. The elevator used in trepanning the skull is also an instrument which is often required in such operations. When we undertake this operation, we should be provided with all the instruments, named, as we cannot always foresee at the commencement of the operation, what instruments we shall need before it is finished.

In some cases, where only a small portion of bone is detached, it may be removed with the common dressing forceps. But in a case where any considerable portion of bone is to be removed, it will be necessary to make an incision in the soft parts to some extent.—The length of the incision required will depend on the length of the sequestra to be removed, which may be estimated by the length of the enlargement of the limb, or diseased part. But, as the sequestra is always shorter than the new-formed bone,

it will not be necessary to extend the incision the whole length of the enlargement; besides, if the first incision should be found insufficient to give us free access to the bone, we can enlarge it at any stage of the operation.

The better mode of procedure is—first, to insert a probe into one of the principal openings, through which the matter issues, or if there is more than one, to insert the probe into that which presents the fairest opportunity to reach the sequestra by an operation, and then to introduce the knife, and carry it upwards (p. 120) as far as may be thought necessary, and if the sequestra extend below the probe, commence another incision from it, downwards, as far as may be deemed proper. The incision should be carried down to the sequestra, if there is no new-formed bone intervening, and if there should be, as is commonly the case, the incision should be carried down to it. It sometimes happens that, though the new bone has formed and partly enclosed the sequestra, yet we find a sufficient space open, or covered only with soft parts, through which we may extract the sequestra; and in order to effect this without sawing away the new-formed bone, it is often necessary to saw, break, or cut, the sequestra into two pieces, for it is often covered by the new bone to some extent, at each end, so that, by cutting it in two pieces, we can withdraw each through a small opening.

I would observe that, in making the incision through the soft parts, we should avoid wounding any artery of considerable size, and especially any tendon. We cannot always avoid wounding the muscles, but if they are divided in the direction of their fibres, no serious evil arises.

The treatment of the wound, after the operation, should be perfectly simple, and similar to the treatment of a simple wound.

When I first began to perform operations of this kind, I was under apprehension lest so much bruising and handling of the soft parts, as is sometimes necessary, to dislodge a large sequestra unfavourably situated, might be followed with bad consequences, and some of these operations have been the most laborious and tedious, both to myself and the patient, which I have (p. 121)

ever performed, yet I have never known any untoward circumstances to follow such operations, of which I have performed a great many.

If the whole of the sequestra is removed, the cure will be perfect; but if any portion of it is left, it will keep up a discharge, somewhat in proportion to the quantity of dead bone left in the limb.

THE END

# MEDICAL CLASSICS

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DOUGLAS ARGYLL ROBERTSON



## Douglas Argyll Robertson

### BIOGRAPHY

- 1837 Born in Edinburgh, son of John Argyll Robertson, M.D., F.R.C.S.E., a lecturer in surgery in the Extra-Academical School and a surgeon interested chiefly in ophthalmic surgery. Douglas had his academic training in Edinburgh and Germany and studied medicine in Edinburgh and at St. Andrews.
- 1857 Age 20. Graduated with M.D. at St. Andrews.
- 1858 Age 21. House surgeon in the Royal Infirmary.
- 1859 Age 22. Studied abroad. In Berlin was influenced by von Graefe, the leading ophthalmologist of the day. Returned to Edinburgh and specialized in ophthalmology. Became an assistant in the University and conducted first class of practical physiology ever held there.
- 1862 Age 25. Fellow of the Royal College of Surgeons of Edinburgh.
- 1867 Age 30. Assistant ophthalmic surgeon to Edinburgh Royal Infirmary until 1870.
- 1868 Age 31. Published papers on pupillary reaction to light and accommodation (Argyll Robertson pupil).
- 1870 Age 33. Appointed full ophthalmic surgeon.
- 1882 Age 45. Married daughter of Mr. W. M. Fraser of Findrach and Tornavein, Aberdeenshire. Had no children.
- 1886 Age 49. Elected President of Royal College of Surgeons of Edinburgh.
- 1887 Age 50. Vice-President of Section of Ophthalmology at British Medical Association meeting in Dublin.
- 1888 Age 51. Honorary President at International Ophthalmologic Congress in 1888 and 1889.



- 1894 Age 57. Presided over International Ophthalmologic Congress in Edinburgh.
- 1895 Age 58. Vice-President of Section of Ophthalmology at British Medical Association meeting in London.
- 1896 Age 59. President of Edinburgh Medico-Chirurgical Society. Given LL.D. by University of Edinburgh.
- 1898 Age 61. President of Section of Ophthalmology of British Medical Association.
- 1904 Age 67. Retired from practice, made his home at Mon Plaisir, St. Aubins, Jersey, because of mild climate.
- 1908 Age 71. November 3 left for India to visit Thakur of India who had studied medicine in Edinburgh in 1888.
- 1909 Age 72. Died January 3 at Gondal, India.

Douglas Argyll Robertson was constantly employed in medical service of hospitals and schools of Edinburgh and in affairs of the College of Surgeons. He was Surgeon-Oculist in Scotland to Queen Victoria and King Edward VII, and was the first surgeon outside London to be chosen President of the Ophthalmological Society of the United Kingdom.

Also: Corresponding Fellow of New York Academy of Medicine.  
 Honorary Member of Royal Medical Society of Edinburgh.  
 Foreign Associate of Society of Practicing Physicians of Prague.

Honorary Member of Neurological Society of New York.  
 Member of Committee of Management of Scottish Joint Board which grants Triple Qualification.

Douglas Argyll Robertson was always keenly interested in golf.

## EPONYM

**PUPIL:** One which is miotic and which responds to accommodation effort, but not to light. *On an interesting series of eye symptoms in a case of spinal disease, with remarks on the action of belladonna on the iris, etc.* Edinburgh Med. Jour., 14: 696-708, Feb. 1869. *Four cases of spinal myosis; with remarks on the action of light on the pupil.* Ibid., 15: 487-493, Dec. 1869.

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## INTRODUCTION

People who argue on the importance of inheritance versus environment can find a good example in Douglas Argyll Robertson. His father was a lecturer in surgery, interested chiefly in ophthalmic surgery; the son at the age of 22, just after graduation from medical school, studied in Berlin under von Graefe, the leading ophthalmologist of the day. Who can say which influence was the stronger to make the younger Robertson specialize in diseases of the eye and attain the leading rôle in his own time? The non-argumentators will say that, of course, with such an inheritance and such an environment only one outcome was possible.

At any rate, Argyll Robertson, after studying in Berlin, returned to his native Edinburgh around 1860, at the age of 23. He became an assistant in the university, teaching physiology. At the age of 30 he became an assistant ophthalmic surgeon to The Royal Infirmary, and during the very next year, wrote the papers which have made his name repeated by every medical student and practitioner.

Douglas Argyll Robertson's first paper, herein reproduced in full, describes an interesting "case which illustrates the connexion between spinal disease and certain conditions of the eye." He discusses the physiology of contraction and dilatation of the pupil and then refers to other writers, namely Bell, Brodie, Romberg and Trousseau, who have mentioned the relation of spinal disease and myosis, but states that their references were merely incidental. In great detail the physiology of the action of atropine on the iris is considered. Robertson then speaks of experiments to determine the action of atropine. In the second paper, which is also reproduced here in its entirety, four patients are described. "In all there was marked contraction of the pupil, which differed from myosis due to other causes, in that the pupil was insensible to light, but contracted still further during the act of accommodation for near objects—." The nature of the associated spinal disease is then discussed, in some cases a definite locomotor ataxia being present, other cases being of a questionable cause. We must remember that these papers were written many years before the Wassermann test was introduced.

Today an Argyll Robertson pupil is almost pathognomonic of syphilis of the central nervous system. Several case reports have appeared in the literature in which this pupil was present in multiple sclerosis, injuries to the spine and polyneuritis. But in many of these reported cases other characteristics were present, such as dilatation of the pupils and retardation of the convergence reaction. L. F. McAndrews (*Archives of Ophthalmology*, 10: 520, October 1933) sums up the problem by saying "Most writers on this subject hold that a real Argyll Robertson pupil has certain definite features, besides the absence of the light reflex, and agree with Bumke and Behr that such a pupil is always a sign of syphilis of the central nervous system."

The third paper herein reproduced, *On the calabar bean as a new agent in ophthalmic surgery*, was written at the age of 26, shortly after starting practice in Edinburgh, and shows that at that early period Robertson was interested in experimental ophthalmology and was training himself to be a keen observer.



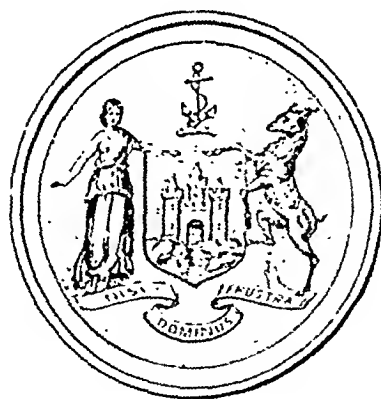


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MDCCCLXIX.



# On an Interesting Series of Eye-symptoms in a Case of Spinal Disease, with Remarks on the Action of Belladonna on the Iris, etc.

BY

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*Lecturer on Diseases of the Eye, Edinburgh*

Published in *Edinburgh Medical Journal*, 14: 696-708, February, 1869



THE following case illustrates the connexion between spinal disease and certain conditions of the eye, and throws light upon some obscure questions of the physiology, pathology, and therapeutics of the eye.

Robert Halkerston, æt. 59, carver, a spare anæmic man, applied for advice on account of dimness of sight in both eyes, but more especially the right, on the 30th of last October.

*History.*—He has suffered from recurrent attacks of inflammation in his *left* eye for the last twenty years, attended by pain in the eye and temple, and dimness of vision. Ever since the first of these attacks the sight in that eye has remained somewhat obscured. He has also at times suffered from pain in it, without any external appearance of inflammation. The other, the *right* eye, suffered from sympathetic irritation when its neighbour was inflamed, but was never the seat of severe inflammation,

and the sight was good in it till a month or six weeks ago, when dimness suddenly supervened, a diffuse uniform mist appearing to envelop objects. This condition has remained without material change to the present time. He has for five years used spectacles of a strength corresponding to his age. He was neither myopic nor hyperopic, and his vision was formerly as good as his neighbours'. From the nature of his occupation his eyes are constantly fixed on his work at a distance of about eighteen inches. He has always been very costive, and is affected with hæmorrhoids, which, however, do not bleed much. He frequently suffers from indigestion and sickness. About two years ago he had a severe attack of frontal tic, and at that time, while out walking one day, he suddenly noticed that he was affected with double vision, which disappeared when one eye was closed. The double vision passed off in the course of a week, and he has had no recurrence of it since. About six months ago, while suffering from frontal tic, he was suddenly seized with giddiness, and with difficulty prevented himself from falling. Two months later he felt his limbs become very weak, while, at the same time, he (p. 697) became affected with cramps in the feet and legs, and numbness as if the limbs were asleep. His gait, too, was unsteady, just as if he had been intoxicated, and he had severe pain in the lumbar region, increased when he walked. His limbs, though still feeble, are, he says, stronger than they were. For several weeks he has had difficulty in retaining his water, and has had to get up at night to avoid wetting the bed; and on taking a drink of water he has generally to go at once to micturate. He states he has no difficulty in making water. He has always been troubled with cold feet in winter. When in the dark, or when he closed his eyes, he noticed he could not stand, but had to grasp at some object for support. He has not observed any failure in the muscular power of his arms. He smokes, but does not, and did not, exceed 2 oz. of twist a week. He used formerly, occasionally, to take ale and spirits to excess, and was then subject to severe headaches. Although affected with "rheumatic" pains, he has never had an attack of rheumatic fever. He is not in the habit of taking opium.

*Examination.*—On examining the eyes, I found both pupils contracted to little more than pin-points, the right rather the smaller of the two. The irides were light-coloured, and apparently healthy in structure. I could not observe any contraction of either pupil under the influence of light, but, on accommodating the eyes for a near object, both pupils contracted. With the intention of dilating the pupil so as to allow of ophthalmoscopic examination, I applied a drop of a solution of sulphate of atropine, of the strength of four grains to the ounce, to the right eye; but, after waiting twenty minutes, I found that the pupil had scarcely dilated at all, so I put another drop of the same solution into the eye, and desired the patient to return the following day for examination. Next day, October 31, I found that the pupil of the *right eye* had become partially dilated, so that it now measured almost  $1\frac{1}{2}$  lines in diameter. It was perfectly circular in form. With this eye he reads very large type (No. xx. of Snellen) at four feet, and large print (No. xii. of Snellen) at one foot distance. On testing him with coloured objects I found that he was quite colour-blind, scarcely recognising the colour of any of a number of objects presented to him. He states that he used formerly to distinguish colours readily. In the *left eye* the pupil was fully half a line in diameter, and circular. There was central nebulous opacity of the cornea of old standing. With this eye he reads very large type (No. xx. of Snellen) at nine feet, and the finest print (No. i. of Snellen) with difficulty at five inches distance. This eye is not so colour-blind as the right, for he can always distinguish blue, and generally the other colours when of a bright tint, although even then he makes occasional mistakes, having a tendency to call all colours of which he is uncertain yellow or gilt. This symptom has been a source of annoyance to the patient, as it prevents him from distinguishing different woods. He has latterly been unable to distinguish between birch and mahogany. On examining the (p. 698) *right eye* with the ophthalmoscope, the media were found quite clear, the optic disc very white and anæmic, but not in the least excavated, the retinal arteries were quite empty and scarcely discernible, appearing as fine light-coloured lines by the

side of the veins, which were partially distended with blood—in fact, there were the appearances which are generally considered indicative of embolism of the retinal artery. Neither eye is abnormally sensitive to light, and vision is best in bright daylight. In the dusk he is not able to see sufficiently to guide himself. His field of vision is markedly contracted in both eyes—being only about twelve inches in diameter at the distance of a foot and a half from the eye.

On applying the stethoscope over the heart, the first sound was heard to be prolonged, but not accompanied by any bruit. There was no tenderness on pressure over the spine.

As I viewed the case as one of considerable medical interest, I asked Dr Sanders to examine the patient, which he kindly did on November 2. He found the heart hypertrophied, the sounds unaccompanied by bruit—the second sound sharp, almost intoned, over the base of the heart. There was marked pulsation in the suprasternal notch. The pulse was hard and full. No tumour nor swelling of any kind was to be observed in the neck. On making the patient close his eyes while standing, he swayed considerably, but did not stagger. In walking his gait was unsteady, especially in turning.

On November 25, the patient returned, and I applied a drop of solution of sulphate of atropine (gr. iv. to ʒi.) to the left eye. In an hour and a half the pupil measured a line and three-quarters, was of a somewhat oval form, but did not exhibit any adhesions between the iris and the lens. A little uveal pigment projected beyond the pupillary margin of the iris. On examination with the ophthalmoscope, the optic disc was found to be slightly cupped, but the interior of the eye otherwise normal. I now put another drop of the solution of the sulphate of atropine into this eye, and a drop of the extract of the Calabar bean into the other, the pupil of which measured fully half a line. After the lapse of an hour and a half the left pupil still measured the same, while the right pupil had contracted so as to measure only a quarter of a line in diameter, and the patient complained that since the application of the Calabar bean the sight in that eye had been much impaired.

I may further mention that there is no perceptible drooping of the lids, the palpebral openings measuring vertically at the centre  $4\frac{1}{2}$  lines, nor have I ever observed any marked flushing of the face, except on one occasion after the patient had been taking more than usually active exercise. The patient himself states that he is not aware of his face flushing more readily than formerly. The sensibility of the face, too, does not appear to be increased.

There are four points in connexion with this case on which I desire to make some remarks—viz.: The myosis or contraction of (p. 699) the pupil; the effect of belladonna and of Calabar bean on the iris; the colour-blindness; and the condition of the retinal vessels.

I. With regard to the myosis.—On first seeing the patient I was struck with the extreme contraction of the pupils, and having previously had one case of myosis apparently dependent on spinal disease under my own care, and seen several such cases while attending Professor Remak's clinique in Berlin, I was led to suspect the dependence of this symptom on a spinal cause—a suspicion which the history of the case verified. The connexion of pupillary contraction with spinal lesions is easily explained by a consideration of the anatomy and physiology of the iris. The iris in the mammalia, as is now universally admitted, contains two sets of nonstriated muscular fibres, the one arranged circularly at its pupillary margin, the other radiating from these circular fibres to the ciliary ligament. By the first the pupil is contracted; it is generally termed the sphincter pupillæ muscle, and is under the influence of the motor oculi nerve. By the second the pupil is dilated; it is usually termed the dilatator pupillæ muscle, and is under the influence of nervous filaments passing from the spinal cord through the cervical sympathetic to the eye. These fibres are usually termed sympathetic, but I incline to consider them true spinal nerves which, though associated with sympathetic filaments, preserve their own individuality. If they are to be viewed as sympathetic, so should the ciliary nerves which pass from the lenticular ganglion to the eye, but which are referred to the third, fifth, or spinal (sympathetic)

nerves, according to the source from which they are derived. In the case just narrated, too, the fibres (so-called sympathetic) which pass to the pupil are those which appear alone to be affected, which is surely an indication that they are distinct from the other filaments; and, as I shall have occasion to mention at another part of this paper, the *vaso-motor* filaments of the sympathetic appear to be paralyzed during the inhalation of the nitrite of amyle, while the *pupillary* fibres remain intact. The fact that division of the cervical sympathetic induced contraction of the pupil was first discovered by Petit in 1727; while Valentin, and subsequently Budge and Waller, pointed out that the filaments connected with the cervical sympathetic passing to the iris were derived from the spinal cord. The latter observers found that the anterior roots of the two lowest cervical and the six upper dorsal nerves supplied these filaments, and to this portion of the spinal cord they gave the term the "cilio-spinal region." The researches of Brown-Sequard<sup>1</sup> show that the limits of this area are often more extended, reaching the level of the sixth, seventh, or even the ninth or tenth dorsal vertebræ. Division of the spinal cord in the upper part of this region was found by Budge to produce dilatation of the vessels of the head and neck, just as if the cervical sympathetic had been (p. 700) divided;<sup>2</sup> and Budge and Waller have also shown that irritation of the spinal cord between the second and third cervical vertebræ occasions still more powerful contraction of the vessels than irritation of the sympathetic.<sup>3</sup> Now myosis may occur as a pathological condition, either from spasm of the sphincter pupillæ, or from weakened action of the dilatator. Apart from inflammatory affections and the use of myotics, we notice myosis as a result of spasm of the sphincter, (1st) in those who, from the nature of their occupation, require to work for lengthened periods at fine objects held close to the eye, in whom the myosis

<sup>1</sup> Lectures on the Physiology and Pathology of the Nervous System, 1860, p. 144.

<sup>2</sup> A dilatation of the vessels of the posterior limb in an animal in whom a lateral half of the spinal cord had been divided, was previously observed by Brown-Sequard in 1857.—Proceedings of the Royal Society, vol. viii. p. 594.

<sup>3</sup> Carpenter's Human Physiology, 1864, p. 232.

is associated with, and dependent upon, spasm of the accommodation, as is occasionally noticed among engravers, jewellers, and watchmakers; and (2d) in cases where the retina is over-sensitive to the influence of light.

Myosis may occur from weakness of the dilatator, (1) where, from pressure of tumours in the neck, the functions of the cilio-spinal filaments are destroyed; (2) in cases of disease of the cord affecting the cilio-spinal region.

In the case narrated, the nature of the man's occupation was not such as to necessitate a very close inspection of his work, and his retina, so far from being over-sensitive, was decidedly dulled to the influence of light, so that the myosis cannot be ascribed to spasm of the sphincter pupillæ. The fact of both pupils being contracted, the absence of any tumour in the neck, and the history of the case, at once exclude the idea of pressure on the sympathetic, and indicate the spinal origin of the myosis.

It is a very curious circumstance that, considering the extent of the cilio-spinal region, injury of any part of which must produce alteration of the pupil, so comparatively few cases of spinal affection are recorded in which this symptom has been observed. I am indebted to Mr. Benjamin Bell for a reference to a case narrated by Sir Benjamin Brodie of a man in whom "there was a small extravasation of blood in the centre of the spinal cord opposite the fifth and sixth cervical vertebræ, and who died in less than forty-eight hours, having been sensible and conscious nearly to the last, but the pupils of his eyes being contracted."<sup>1</sup> Mr. Bell, in a paper in the "Edinburgh Medical Journal" for 1857,<sup>2</sup> also alludes to a case of Dr. Budd's, in which, in consequence of an accident, the spinal cord was converted into red pulpy matter for an inch and a quarter opposite the root of the fifth cervical nerve. The patient died after seven days, and latterly the pupils were contracted. Romberg,<sup>3</sup> in his standard work on the nervous system, makes a mere incidental allusion to the fact that, "in tabes dorsalis, he has (p. 701) found

<sup>1</sup> Medico-Chirurgical Transactions, vol. xx. p. 149.

<sup>2</sup> Vol. ii. p. 30.

<sup>3</sup> Translation published by Sydenham Society, vol. ii. p. 298 and p. 397.



the pupil contracted to the size of a pin's head." At another place, however, he states that he has in *tabes* repeatedly found a change in the pupils of one or both eyes, consisting in a contraction with loss of motion, which attained to such a height in one case, that the pupils were reduced to a pin's head. I notice too, that, in a case of spinal hemiplegia narrated by Dr. Todd,<sup>1</sup> a slight difference in the size of the pupils was observed; which, however, he viewed as the only symptom of *brain* affection in the case.

Trousseau<sup>2</sup> states that he has often noticed, in cases of progressive locomotor ataxy, in the intervals when the patients are free from pain, an injection of the conjunctiva (sometimes conjunctivitis and chemosis), with contraction of the pupil, reducing it to the smallest possible size, and so powerful sometimes that it resists the influence of belladonna. He further mentions that, during the paroxysm of pain, the contraction is replaced by more or less dilatation of pupil, and generally also the injection of the conjunctiva disappears. Dr. Bazire<sup>3</sup> never found the pupils, however contracted, to resist the dilating effect of atropine, nor has he observed dilatation to occur during a paroxysm of pain, nor was there any injection of the conjunctiva on sclerotic. He mentions, however, that Duchenne has published cases in which these phenomena were present in the intervals between the pains, and disappeared during the paroxysms. Dr. Radcliffe,<sup>4</sup> in two cases of locomotor ataxy, observed that the eyes ceased to be bloodshot, and the pupils opened when the pain reached a certain degree of severity and had continued for a certain time, but not otherwise. Stellwag von Carion, in his work on Diseases of the Eye,<sup>5</sup> mentions, among causes of the paralytic form of myosis, *tabes dorsalis* and spinal paralysis. Soelberg Wells,<sup>6</sup> too, notices the fact that the "myosis due to paralysis of the dilatator pupillæ is met with in those spinal

<sup>1</sup> Clinical Lectures on Paralysis, etc., 1856, p. 338.

<sup>2</sup> Clin. Medicine, Bazire, vol. i. p. 149.

<sup>3</sup> *Op. cit.*, p. 205.

<sup>4</sup> Reynold's System of Medicine, vol. ii. p. 345.

<sup>5</sup> English translation, 1868, p. 642.

<sup>6</sup> Treatise on Diseases of the Eye, 1869, p. 164.

lesions in which the sympathetic nerve is affected, so that its influence on the radial fibres of the iris is impaired."

Brown-Sequard, in the admirable lectures at present being published in the "Lancet,"<sup>1</sup> has clearly pointed out the frequent occurrence of higher temperature and increased sensibility of the face and neck, partial closure of the lids, and constricted pupil in cases of spinal hemiplegia, on the side corresponding to the lesion. In three out of seven illustrative cases that he narrates, constriction of the pupil was observed. I am not aware that a variation in the size of the pupil has been noticed in any of the many cases of spinal injury or concussion of the spine resulting from railway accidents, but it appears to me that very weighty positive (p. 702) confirmation might be afforded by the presence of this symptom in cases otherwise doubtful.

A contracted state of one of the pupils is now generally recognised as a common symptom of the presence of a tumour in the neck, interfering with the functions of the sympathetic. The credit of first pointing out the connexion between a myosis and cervical tumour is, I believe, due to Dr. John Reid, who, in a paper in the "Edinburgh Medical and Surgical Journal" for 1841, refers to a case narrated in the "Medical Gazette" for September 1838, where a large tumour involved the carotid, vagus, and surrounding parts, and where the sympathetic could hardly be supposed to escape, and in which the pupil is described as having become smaller in the course of the disease. Dr. F. von Willebrand,<sup>2</sup> in 1854, related a case of unilateral myosis depending on the pressure of enlarged lymphatic on the cervical sympathetic. As the enlargement of the glands subsided under treatment, the pupil became more dilated, until it eventually resumed its natural size. Professor Gairdner<sup>3</sup> has directed special attention to this symptom in cases of aneurism at the root of the neck, and has related several such cases. Dr. Grainger Stewart showed that this condition existed in a remarkable case of lordosis which he brought before the Edinburgh Medico-Chirurgical Society in July last.

<sup>1</sup> See "Lancet" of November 7th and 21st, and December 12th, 1866.

<sup>2</sup> Archiv für Ophthalm., band i. abth. i. p. 319.

<sup>3</sup> Edin. Med. Journal, January and August 1855.

II. The second point to be noticed is the effect produced upon the iris by atropine and the Calabar bean.

Atropine induced dilatation of the pupil, but only to about medium size, thus falling far short of its usual effects; and although reapplied it failed to produce any further change. Its action, moreover, was somewhat transient, even the limited dilatations soon disappearing. This want of susceptibility in the iris to the action of belladonna in cases of myosis has been previously observed, and is referred to by Mackenzie,<sup>1</sup> Trousseau,<sup>2</sup> and Wells.<sup>3</sup>

Calabar bean produced further contraction of the pupil, reducing its diameter to rather less than one-fourth of a line, an amount of contraction greater than I have seen it produce in any other case.

These actions appear to me to throw some light upon the theory of the effects of these agents; but in order to make this plain, I shall briefly indicate the different theories that exist on this subject, the data on which they were founded, and the objections that may be brought against each.

1. Dr. Fleming maintains<sup>4</sup> the view that the iris is an erectile tissue, and that the size of the pupil may be determined by the state of its vessels. He considers that atropine constricts the arteries of the iris, relaxing that membrane, and this constriction (p. 703) and relaxation draws into action, by what he terms functional sympathy (without intervention of brain or cord), the radiating fibres, and dilates the pupil. He bases his theory very much on a series of experiments made by Mr. Wharton Jones which demonstrated that the application of a solution of the sulphate of atropine to the web of a frog's foot induced contraction of the arteries. He also states in corroboration of his view that atropine has no action on the iris of a dead eye. But, in opposition to these views, I would remark that Schneller<sup>5</sup> points out

<sup>1</sup> Treatise on Diseases of the Eye, 1854, p. 883.

<sup>2</sup> *Op. cit.*, p. 149.

<sup>3</sup> *Op. cit.*, p. 164.

<sup>4</sup> Inquiry into the Action and Uses of Atropia. Edin. Med. Jour., March 1863.

<sup>5</sup> Ein Mikrometer am Augenspiegel, etc. Archiv für Ophthal., band iii. abth. ii. p. 155.

that atropine occasions distention of the vessels of the choroid, and he maintains of the vessels of the iris also. This action he ascribes to paralysis of the ciliary muscle, whereby the intra-ocular pressure is reduced. By means of an ingenious arrangement, he was enabled to measure exactly the size of the vessels in the interior of the eye, and he made very numerous experiments which placed it beyond doubt that the size of the vessels of the choroid was regulated by the amount of intra-ocular pressure, and that atropia, like paracentesis of the cornea and division of the external muscles of the eyeball, dilated the vessels by diminishing the intra-ocular pressure.

Clinical observation also leads me to doubt the correctness of Dr. Fleming's views, as in a case of glaucoma, in which the pupil was greatly dilated, I found the vessels of the iris extremely distended. Kussmaul<sup>1</sup> also found that when the iris was distended with blood or emptied of it, the pupil still dilated and contracted under the influence of light, and that the pupil may be either contracted or dilated when the iris is in very different states of vascular injection. Moreover, I have satisfied myself by repeated observations, that while nitrite of amyle occasions distention of the vessels of the head and neck it does not occasion any constriction of the pupil. I have frequently observed, on administering nitrite of amyle to rabbits, that while increased injection of the membrana nictitans was distinctly observable, the most careful measurement failed to reveal the slightest alteration in the size of the pupil.

Dr. Fleming, too, is mistaken in the statement that atropine does not act on the iris of the dead eye, as numerous experiments have shown that atropine acts on the iris for some time after the eye-ball has been excised. This is of course fatal to his view.

Donders<sup>2</sup> has also observed the vessels of the iris to contract on irritation of the sympathetic nerve even when, after the action of the Calabar bean, the same irritation scarcely makes the pupil dilate. We are thus forced to conclude, that the state of

<sup>1</sup> Quoted by Schneller. *Loc. cit.*, p. 132.

<sup>2</sup> Accommodation and Refraction of the Eye, p. 580.

distention of the vessels of the iris has no marked influence on the size of the pupil.

2. Another view which has been most ably maintained, among others by Mr. Benjamin Bell,<sup>1</sup> is that atropine acts by stimulating (p. 704) the radiating fibres to contraction. He founds this view chiefly upon the fact that, in cases of complete paralysis of the third pair when dilated pupil, atropine induces further dilatation, and that when the cervical sympathetic is divided no contraction ensues in a pupil fully dilated by atropine.

Dr. Harley,<sup>2</sup> in two communications published in reply to Mr. Bell's, relates some experiments in which he divided the sympathetic in the neck, and applied atropine to the cut extremity without producing any effect on the pupil. He also divided the third nerve in a cat, and induced great dilatation, which was not increased by atropine, and on thereafter dividing the cervical sympathetic the pupil returned to a medium size. From these observations he concluded that atropine acts purely by paralyzing the sphincter pupillæ. Harley also divided the cervical sympathetic in the neck after having dilated the pupil thoroughly with atropine, and found that no change was induced in the size of the pupil, but rather views this as corroborating the notion that dilatation depends upon excitation of the radiating fibres. In opposition to the view that atropine acts by stimulating the dilatation merely, we have the fact that atropine administered internally induces paralysis of the motor nerves, affecting first their peripheral extremities.<sup>3</sup> Again, when locally applied to the eye, it induces paralysis of the muscle of accommodation, which is supplied by filaments of the same nerve as the sphincter pupillæ.<sup>4</sup> That the dilatator is irritated is also nega-

<sup>1</sup> Edin. Med. Journal, vol. ii. pp. 30, 521, and 815.

<sup>2</sup> Edin. Med. Journal, vol. ii. pp. 431 and 705.

<sup>3</sup> Botkin, Ueber die Physiol. Wirkung des Schwefels. Atropins. Virchow's Archiv, band xxiv. p. 83.

<sup>4</sup> That the third is the nerve of accommodation is now almost universally admitted, and is indicated by the fact, that in complete paralysis of that nerve the power of adjusting the eye to distances is always limited, while the experiments by Dr von Frautvetter (Archiv f. Ophth., band xiii. abth. i. p. 95) have positively demonstrated that in birds, when the third nerve is irritated, the lens becomes more convex, while irritation of other nerves fails to produce any effect on that structure.

tived by the fact pointed out by Budge, that belladonna still acted on the pupil thirteen months after the sympathetic had been divided on that side, and where shortly after death galvanism did not induce dilatation of the pupil as it did in the other eye. The pupil, also, when dilated is immobile, which is rather indicative of a state of paralysis than of spasm. The facts that dilatation of the pupil may be kept up for years, and that even the direct application of galvanism cannot induce contraction in a pupil dilated by atropine, which under ordinary circumstances it would strongly do, are surely indicative of a paralytic change.

3. Some writers suppose that atropine acts simply by paralyzing the sphincter pupillæ.<sup>1</sup> Against this it has been urged, that in paralysis of the third pair with dilated pupil atropine induces (p. 705) further dilatation, but this reasoning is not conclusive, because in many cases the paralysis is not complete; and even when the paralysis is complete, unless it be of long standing, the peripheral extremities of the nerve may still retain their sensibility and be capable of being further paralyzed by atropine. That this may occur is evident from the fact, that in excised eyes where all the nerves passing to the iris are removed from their central connexions, atropine still acts. Another objection raised to this view is, that in birds, in whose irides no dilatation exists, atropine does not induce more than a temporary dilatation. But this also is somewhat fallacious, because in birds, where the muscular fibres of the iris are striated, a different type of organization may reasonably be held to exist. Another objection, advanced by Ruyter,<sup>2</sup> is, that on dividing the sympathetic in a rabbit in which the pupils are dilated and stimulating the cut extremity, no further dilatation ensued. But this experiment has been performed by others with the opposite result; while Zelenski has shown that, though the pupil be fully dilated by atropine, if the animal be poisoned with woorara, at the moment of death still further dilatation ensues, pro-

<sup>1</sup> Budge, Ueber die bewegungen der Iris, etc., 1855; Braun, Archiv f. Ophthalm., 1866, abth. ii. p. 112; Hirschmann, Reichert et Du Bois-Reymond's Archiv, 1873, p. 27.

<sup>2</sup> De Actione Atropæ Belladonnæ in Iridem. Quoted by Cremat.

ing that the dilatator if stimulated is capable of still further stimulation. Czermak<sup>1</sup> made a series of experiments which, at first glance, seemed to prove the action of atropine on the radiating fibres. He rapidly removed the cornea from a rabbit which he had just killed, and cut out the circular fibres of the irides, leaving the dilatators intact; he then applied to the one eye a strong solution of the sulphate of atropine, and to the other distilled water. After a time the pupil to which the atropine had been applied was found to be more dilated than the other, from which he concluded that the radiating fibres were stimulated by the atropine to contraction. His reasoning was, however, fallacious, as the increased contraction of the muscle might be due to the direct irritating action of a saline solution. Kölliker,<sup>2</sup> too, had performed similar operations with different results. The only circumstance which, in my opinion, favours the view that atropine stimulates the radiating fibres to contraction is the degree of energy with which dilatation occurs, as exhibited by the tearing through of adhesions between the iris and the lens, which is much beyond what we would naturally ascribe to the simple removal of an antagonistic force.

4. Some writers ascribe the action of atropine to a combined effect, paralysis of the sphincter and stimulation of the dilatator.<sup>3</sup> Von Graefe has related a most interesting case of tumour at the base of the brain, in which complete paralysis of the third, fourth, fifth, and sixth nerves on the right side occurred. The pupil was slightly (p. 706) dilated and immobile, and became fully dilated under the use of atropine. From this Von Graefe concludes that atropine acts on the dilatator fibres. At a later period the *left* oculo-motor and trochlear nerves became also paralyzed, and there was *complete* dilatation of the left pupil, which complete dilatation Von Graefe describes as "active" and dependent on coexistent irritation of the sympathetic branches at the base of the skull. Would it not, however, be

<sup>1</sup> Kleine Mittheilungen aus dem k. k. Physiol. Institute in Pesth, zweite und dritte reihe. Moleschott's Untersuchungen, band vii. 1861.

<sup>2</sup> Zeitschr. f. Wissensch. Zoologie, band vi. 1855, p. 143.

<sup>3</sup> Czermak, *loc. cit.*; Von Graefe, Archiv für Ophthalm., band vii. abth. ii. p. 24.

more natural to ascribe the imperfect dilatation of the right pupil to partial paralysis of the ciliary branches of the third, rather than suppose concomitant irritation of the sympathetic to account for the complete dilatation of the left pupil? Against Von Graefe's view may be reasonably urged the improbability of the same substance exerting contrary actions on identical tissues, while the arguments previously adduced against the theory, that atropine stimulates the radiating fibres, applies of course also to this.

5. It may seem strange, but some authors maintain that these disputed phenomena are referable to paralysis of both nerves and both muscles.<sup>1</sup> This view is founded on the fact, that galvanism applied to the eye immediately after death gives rise to contraction of the pupil, but after a short time induces on the contrary dilatation.<sup>2</sup> This would favour the conclusion that the irritability of the motoroculi nerve was sooner lost than that of the cilio-spinal. This being the case, atropine is supposed to act by paralyzing both nerves, but the third being more readily affected than the cilio-spinal, dilatation ensues. The energetic dilatation of the pupil tells strongly against this view; and also the fact, that strong doses of atropine, or repeated applications, tend to induce increased dilatation, whereas if it paralyzed both nerves in different degrees, and one subsequently to the other, one would expect a prolonged or free use of atropine would bring the pupil to a medium size.

6. The last point to which I shall refer is a view propounded by Ludwig, and supported by many, that the atropine acts directly on muscle.<sup>3</sup> This is a question which it is almost impossible definitely to resolve with our present knowledge, because the peripheral extremities of the nerves are so intimately associated with the muscles that it is impossible to separate the actions of agents on muscles from those on nerves. Zelenski,<sup>4</sup> from a

<sup>1</sup> Zelenski, Zur Frage von der Muskelirritabilität. Virchow's Archiv, band. xxiv. p. 362.

<sup>2</sup> Ruyter, *op. cit.*

<sup>3</sup> Harley, Edin. Med. Journal, vol. ii. p. 705.

<sup>4</sup> *Op. cit.*



series of very carefully performed experiments with woorara, arrived at the conclusion that an independent muscular irritability is not proven to exist.

In considering the bearings of our case on these different theories, we must keep in mind that in it we have perfect paralysis of the radiating fibres of the iris.<sup>1</sup>

(p. 707) With regard to Dr. Fleming's view, it is sufficient to state that our case supplies no facts tending to support it. The second theory, that atropine acts purely by stimulating the radiating fibres, is, I think, demonstrated to be erroneous; because if such were the action of atropine in our case, one would not expect a mere medium dilatation of the pupil. For in cases of myosis from spasm, either idiopathic or induced by the Calabar bean, we find atropine to produce its full effects. Thus the diminished effect of atropine contrasts strongly with what I have observed to occur in a case of dilated pupil, the result of paralysis of the sphincter pupillæ of long standing, in which the Calabar bean effected an extreme contraction of the pupil. The view that atropine acts by paralyzing the circular fibres receives considerable confirmation, as by this view the effects produced can be best explained. The radiating fibres being originally paralyzed, the pupil is brought to a state of medium dilatation by paralyzing the remaining fibres. Were the view correct, that the circular fibres are paralyzed by belladonna, and the radiating at the same time stimulated, we would, from what I have noticed in the action of the Calabar bean in mydriasis of long standing, look for a dilatation of the pupil in our case somewhat beyond medium size. The case narrated throws no particular light upon the truth or fallacy of the other views.

Where facts and theories are both conflicting, and in many cases contradictory, it is not easy to arrive at a true solution of the problem. With the view of coming to a determinate con-

<sup>1</sup> That the myosis was not due to increased distention of the vessels of the iris is, I think, evident from the fact that no such distention was visible either in the iris itself or neighbouring parts, and also the curious fact, that while the right pupil was somewhat more contracted than the left, the supply of blood to the right eye by the ophthalmic artery appears to have been obstructed. (The reasons for this supposition are given further on.)

clusion on this point, I performed a number of experiments, but found that in each I had been forestalled by previous observers. The most important fact that I elicited from one experiment was a confirmation of Ruyter's view, that stimulation of the cervical sympathetic does not occasion increased dilatation of a pupil fully under the action of atropine; but this requires confirmation. Should it prove correct, I would be inclined to the view that atropine, though it acts mainly by paralyzing the sphincter pupillæ, may perhaps secondarily stimulate the dilatator. By another series of experiments with woorara, I obtained similar results to those detailed by Zelenski.

The effect of the Calabar bean in the case of our patient serves to corroborate the view I originally advanced,<sup>1</sup> that it acts, not by paralyzing the radiating fibres,<sup>2</sup> but by stimulating the circular, as here the dilatator was evidently completely paralyzed.

III. The *colour-blindness* is not an unfrequent symptom of advancing amaurosis, and I believe would be found to exist far more commonly than is supposed, were patients more frequently tested on the point, as it is well known that they are often themselves (p. 708) unaware of their defect. As particularly bearing upon our case, I may mention that Dr. Moritz Benedict<sup>3</sup> states, that during two years he has very frequently observed colour-blindness, especially of red and green, along with the amaurosis, accompanying tabes. He narrates six cases in which he found colour-blindness and amaurosis combined, but in none of these were there well-marked signs of spinal disease. A most interesting case bearing upon this subject is narrated by Mr. Poland.<sup>4</sup> A corn-factor brought an action for damages against a railway company on account of injuries received in a collision on their line. In addition to some bruises over the spine, a contusion over the temporal bone and on right shoulder, with loss of power in the arm, the patient complained of numb-

<sup>1</sup> The Calabar Bean as a New Agent in Ophthalm. Medicine. Ed. Med. Journal, March 1863.

<sup>2</sup> Dr T. R. Fraser on the Ordeal Bean of Calabar. Ed. Med. Journal, July, August, and September 1863.

<sup>3</sup> Der Daltonismus bei Schnerven-Atrophie. Archiv f. Ophth., band. x. abth. ii. p. 115.

<sup>4</sup> Roy. Lond. Ophth. Hosp. Reports, vol. iii. p. 259.

ness of the lower extremities, great depression of spirits, and coloured vision, all objects appearing yellow to him. This last symptom of course seriously interfered with his business, and the jury awarded him £1200 damages. Dr. George Wilson<sup>1</sup> narrates a case of colour-blindness resulting from a fall from a horse, which was followed by severe nervous symptoms. It would be well, I think, if more attention were paid to this symptom in spinal and other nervous affections.

IV. The condition of the Retinal Vessels.—The rapidity with which the blindness occurred in the patient's better eye, and the appearances revealed by the ophthalmoscopic examination, sufficiently indicated the nature of the lesion. From some careful anatomical and pathological observations and researches of Dr. Steffan,<sup>2</sup> it would appear that the term embolism of the arteria centralis retinæ is not strictly applicable to this and similar cases; for if that artery merely be obstructed, the collateral circulation is sufficiently free to fill the retinal vessels to almost their natural calibre. The cases therefore of complete arterial obstruction are, he maintains, in reality cases of embolism of the *ophthalmic* artery. The fact that the amaurosis depended upon embolism renders it not at all improbable that the spinal affection may be due to a similar cause—a hypothesis which the occurrence of some improvement in the patient's symptoms serves to strengthen.

THE END

<sup>1</sup> Researches on Colour-Blindness, 1855, p. 38.

<sup>2</sup> Ueber Embolische Retinalveränderungen. Arch. f. Ophth., band. xii. abth. i. p. 34.



# Four Cases of Spinal Myosis; with Remarks on the Action of Light on the Pupil

BY

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**A**TAILOR, George Smith, æt. 51, applied to me for advice on account of dimness of sight. He stated that he enjoyed good health until July last year, when one very hot afternoon, while crossing the North Bridge, he felt giddy and faint, but managed with some (p. 488) difficulty to walk home. The following day he experienced pain in his back, extending to his legs, increased while taking exercise. His back was also tender on pressure. He had, moreover, twitchings, and occasional numbness in his legs, especially the right, with want of power, so that in walking he staggered, and had to use a stick. He could not stand steadily in the dark, but had to grasp at some object for support. He at this time complained of dull pains in his forehead, and noticed that his water constantly dribbled away. These symptoms prevented him continuing more than a few hours daily at work. He did not observe his sight affected till the end of December, when he discovered that the sight in his right eye was dim. Since then the sight has neither improved nor deteriorated, while with his left eye he sees as well as he ever did, but he has noticed that objects appear darker than they used to do, and that he requires

more light while working than formerly sufficed. He is not conscious that his face flushes more readily than natural.

On examination, I found that while walking his gait was unsteady, and that he could not plant his feet firmly on the ground. He also exhibited considerable awkwardness in turning. He stood erect with his eyes closed, but swayed a little from side to side. On looking at the eyes, the drooping of the lids and the small size of the pupils at once attracted attention. The drooping of the lids was more marked in the left than the right eye—the left palpebral aperture at the widest point measuring only  $3\frac{3}{4}$  lines, while the right measured 4 lines. Each pupil measured  $\frac{3}{4}$  line in diameter; they were insensible to the influence of light, but contracted to  $\frac{1}{2}$  line during the act of accommodation for a near object. Under repeated instillations of a strong solution of sulphate of atropine, the right pupil became dilated to a little beyond medium size, so that it measured  $2\frac{3}{4}$  lines in diameter, and was quite immobile.

With the right eye the patient was slightly myopic, but even with a suitable glass had difficulty in making out very large print (No. LXX. of Snellen) at 20 feet distance. With the left eye vision was normal (No. XX. at 20 feet).

With the ophthalmoscope a slight degree of atrophy, with shallow cupping, of the right optic nerve was discovered. From the very small size of the pupil, the interior of the left eye could not be examined. Under the use of iron, combined with small doses of strychnia, a considerable improvement occurred in most of the patient's symptoms, but the pupils remained contracted, and the sight in the right eye unaltered.

For notes of the history and general symptoms of the following case, and for bringing the patient under my notice, I am indebted to my friend Dr. Sanders.

John Grey, æt. 35, a clerk, was admitted to the Royal Infirmary on the 11th of June 1869, complaining of weakness in his legs and right arm.

(p. 489) He always enjoyed good health until fifteen years ago, when he contracted syphilis. He has never had any erup-

tion, nor sore throat, but suffered from a swelling over his right ulna, probably of periostitic nature, which disappeared under the use of iodide of potassium. He resided for a year in India, and shortly after his return, nine years ago, he had an attack of hemiplegia, which affected the left side of the face and right side of the body. Twelve months afterwards, when nearly convalescent, he consulted Dr. Christison for convergent squint of his left eye, and was ordered some mercurial pills, and, while taking them, he states that he caught cold, to which he refers the commencement of his present disease.

The patient is a man of middle height, somewhat emaciated; has large joints and florid cheeks. There is very marked contraction of pupils. They each measure half a line in diameter, are insensible to light, but contract during the act of accommodation for near objects. There is no drooping of the eyelids. The skin is cool, soft, and moist. The temperature of the inferior extremities, more especially the right leg, is below that of the body. There is diminution in the motor power of both legs, accompanied by a feeling of stiffness. He can move them in all directions, but not actively. He can stand pretty steadily, even when the eyes are closed; but when he does so, he bends his body forwards, while his legs are curved slightly backwards at the knee-joints. He walks with a peculiar straddling gait. The muscles of his right calf and thigh are smaller than those of his left. There is no atrophy of the deltoid. There is partial anæsthesia, without analgesia in the right iliac and inguinal regions, extending down the right leg. Reflex action is very marked in right leg—so much so, that it often starts up without any apparent stimulus. Motor power in the right arm and hand is diminished, so as to prevent the patient carrying on his occupation as clerk. He does not complain of headache, but considers his memory affected.

The patient's vision is very slightly affected. With either eye he is able to read fine print, and is able to distinguish colours perfectly. To permit of ophthalmoscopic examination, and to test the extent to which the pupil will dilate, a drop of a 1 per cent solution of atropine was introduced into the left eye. The

lowing day the left pupil measured two lines in diameter. With the ophthalmoscope a slight degree of "cupping" and lighter colour of the optic disc, indicating a little atrophy of nerve substance, was the only pathological condition discovered.

Dr. G. W. Balfour directed my attention to the following two cases, and kindly supplied me with notes of their history and the results of examination into their general, and more especially their nervous, symptoms:—

John Dann, æt. 43, iron-turner, was admitted to the Royal Infirmary May 12, 1869, complaining of a staggering and inability to (p. 490) walk, a difficulty in making water, and dimness of sight after reading for a time.

About six years ago he was seized with pain in his bladder, which was so severe as to compel him to leave his work. This pain returned at intervals of a month or two, after which he noticed that he could not make his water freely, and eventually that it dribbled away at night. He applied to a local practitioner for relief, and was treated for paralysis of the bladder, and subsequently for stricture. He was next treated at the Newcastle Infirmary for stricture and diseased prostate, and after two months was discharged as cured. He soon thereafter felt that he staggered, and could not walk straight in the streets, and observed, while washing his face, that, on shutting his eyes, he could not help falling forwards on to the basin. He once more applied for advice at the Newcastle Infirmary, and was again treated for enlarged prostate; but obtaining no benefit from the treatment pursued, he was sent to the Edinburgh Royal Infirmary to the care of Dr. Watson, because of supposed prostatic disease. Finding it to be a case of nervous affection, Dr. Watson transferred the patient to the Medical House. The patient has for five years past had severe pains in the rectum, to allay which he used to employ laudanum injections, but has desisted from their use since January last.

Dr. Balfour found, on careful examination, that the skin of the trunk and extremities was insensible to pain, except in a narrow zone extending round the body, its breadth corresponding

to the distance between the sixth and twelfth dorsal vertebræ. Sensibility in this zone is not increased. Electro-mobility and electro-sensibility were unimpaired. He complained of the sensation of a tight cord round his waist. He walks somewhat feebly, and staggers on turning. He also sways considerably if he closes his eyes while standing, and would fall if he did not open his eyes, or grasp some object for support.

On examining his eyes I found the left pupil more contracted than the right; the left measuring  $\frac{3}{4}$  line, the right 1 line in diameter. There is a tendency to divergent strabismus of the left eye, for when the patient looks fixedly at an object about a foot from the eye, the left eye is seen after a time to roll outwards. Vision in the right eye is perfect, but with the left only moderate-sized print can be read. The pupils are insensible to light, while atropine only occasions medium dilatation (to 2 lines). On ophthalmoscopic examination both optic nerves were found considerably injected; while in the left eye there was a peculiar congenital abnormality, a portion of the sheaths of the optic nerve fibres passing beyond the fascia cribosa, and extending over the retina upwards and outwards from the optic disc for a distance about equal to the diameter of the optic disc. In other respects, the fundus of both eyes is normal.

Under the use of nitrate of silver in  $\frac{1}{2}$  gr. doses, the patient considerably improved during his residence in the Infirmary.

(p. 491) The following case is at present in Dr. Balfour's wards. Although it is certainly not a typical example, I here include it, because the myosis is well marked, presenting similar features to the contracted pupils in the other cases, and because there are some slight and obscure nervous symptoms which *may* be indicative of incipient spinal affection.

Robert Clerk, æt. 66, a clerk, was admitted into Dr. Balfour's wards on 18th October 1869, complaining of general debility. His appearance sufficiently indicates that for a lengthened period he has been in straitened circumstances. He, however, enjoyed good health till three years ago, when he suffered from varicose ulcers on his legs, which, under treatment, disappeared in about six months. Since that time he has never completely regained



his strength, although he thinks he has improved of late. For the last two or three years he has been troubled with twitchings and startings of the legs while in bed at night, and for three months he has experienced a great heat in the skin, especially of the legs. He has no incontinence of urine, but states that he cannot expel his water with any force.

On examination no decided impairment of muscular power or of sensation could be anywhere detected. His gait, however, is unsteady, and when he stands with his feet close together and shuts his eyes, his body sways somewhat, but he can stand thus without support for some time.

Both pupils are of the same size, and markedly contracted, measuring barely 1 line in diameter, and only partial dilatation (to  $2\frac{1}{2}$  lines) ensues on the application of a strong atropine solution. No alteration in the size of the pupil is observable under the influence of light, but when near objects are looked at contraction at once ensues. Vision is good, though not perfect in both eyes, and there is no colour-blindness.

On ophthalmoscopic examination a slightly atrophic condition of the optic nerves was observable.

(I may mention that in the examination of this patient considerable difficulty was experienced in getting from him an accurate account of his history and symptoms, as he exhibited a great tendency to modify his statements to what he imagined would please his examiner.)

These four cases serve well to illustrate the connexion between certain eye-symptoms and a diseased condition of the spinal cord. In all of them there was marked contraction of the pupil, which differed from myosis due to other causes, in that the pupil was insensible to light, but contracted still further during the act of accommodation for near objects, while strong solutions of atropine only induced a medium dilatation of the pupil.<sup>1</sup> In three of the (p. 492) cases a slight degree of atrophy of the optic nerves

<sup>1</sup> I may mention, that the patients have been frequently carefully examined as to these points with a like result by Mr Walker, Professor Sanders, Dr G. W. Balfour, Dr Barde of Geneva, and many others.

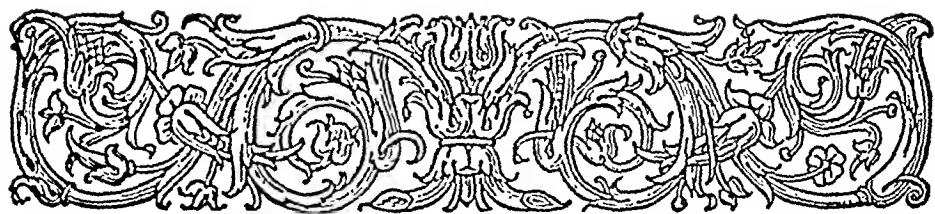
existed, as was evinced by a shallow excavation and lighter colour of the optic disc. In one, we observed a symptom which has been noticed occasionally in spinal disease by Brown-Sequard and others—namely, a drooping of the upper lids. In none of the cases was there any appreciable colour-blindness. As regards the nature of the spinal lesion, in one case the characters of locomotor ataxy were well marked; in the other two the form of spinal affection is doubtful; while in the fourth patient, as I have already mentioned, the symptoms of spinal disease are by no means well marked.

To most of the eye-symptoms found in these cases I alluded at length in a previous communication to this Journal. I will therefore pass them over without remark at this time. But I now desire to direct special attention to a very remarkable circumstance which I noticed in the case that formed the subject of my previous paper, and which I again observed in all the above cases, viz., that although the retina is quite sensitive, and the pupil contracts during the act of accommodation for near objects, yet an alteration in the amount of light admitted to the eye does not influence the size of the pupil. This cannot be explained by the supposition that the pupil is already so small as to be incapable of further contraction under light; because (in the healthy eye) a still further degree of contraction of the pupil may be effected by the use of the Calabar bean, and yet the pupil varies in size according to the intensity of the light. The only possible solution of the difficulty is to be found in the theory, that for contraction of the pupil under light it is necessary that the cilio-spinal nerves remain intact, and, as in these cases of myosis the cilio-spinal nerves are paralyzed, light does not influence the pupil. But hitherto this contraction of the pupil under light has been invariably referred to reflex stimulation of the ciliary branches of the third pair which supply the circular fibres of the iris. If this latter view were correct, I see no reason why in these cases light did not influence the pupil. In all of them the retina was thoroughly sensitive to light, and in all of them the ciliary branches of the third pair were healthy and active (as was shown by the further contraction of the pupil

during the act of accommodation, which can only be referred to these nerves). But in all there were symptoms of spinal disease, and in all myosis due to paralysis of the cilio-spinal nerves. I am therefore inclined to the former view, in which case it is necessary to assume that the contraction of the pupil which naturally occurs when light is admitted to the eye is not as has been hitherto supposed an excellent example of reflex action, but an isolated example of normal, temporary, reflex paralysis.

I am aware that a dilated immobile condition of the pupil has been found to follow division of the third pair in animals, and that in cases of complete paralysis of the third pair, the pupil is dilated usually and insensible to light. This would rather tend to (p. 493) the conclusion that the contraction of the pupil under light is due to the motor oculi; but in division of this nerve, so many tissues are injured at the same time as to render deductions from effects observed open to many fallacies, while in cases of paralysis of the third pair, we not unfrequently observe the pupil to act partially under the influence of light; and where this is not the case, the immobility may be due to degenerative changes in the nervous or muscular tissue. For a thorough solution of this question, further experiments and clinical observation are necessary.

THE END



# On the Calabar Bean as a New Agent in Ophthalmic Medicine

BY

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(The substance of this paper was read as a communication at a meeting of the Edinburgh Medico-Chirurgical Society, on 4th February 1863.)

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**F**OR more than a year I have recognized the numerous advantages that would flow from the discovery of a substance which, when applied to the conjunctiva, should produce effects exactly opposite to those well known to result from belladonna or atropine; which should stimulate the muscle of accommodation and the sphincter pupillæ as the above-named remedies paralyze them. With the view of discovering such an agent, I endeavoured to ascertain from experiments of my own, and from the writings of previous observers, whether any of the common vegetable principles possessed this property. These investigations were, however, productive of no satisfactory results, until my friend Dr. Fraser informed me that he had seen contraction of the pupil result from the local application of an extract of the ordeal bean of Calabar. I resolved to investigate the action of this substance, and, above all, to ascertain whether it extended any influence on the accommodation of the eye. With some difficulty I got a few Calabar beans, and, with the view of obtaining their active principles in a convenient form, prepared from them

three extracts of varying strengths in the following manner:—The weakest of the three was made by thoroughly digesting gr. xxx. of the powdered Calabar bean in alcohol, carefully evaporating the strained fluid to dryness, and then adding to the residue one dram of water. This formed a muddy solution of a light reddish brown tint. In strength, one minim of this solution corresponded to about half a grain of the bean. The second extract was formed by evaporating a portion of the first to about a quarter of its volume; so that one minim of this extract corresponded to about two grains of the bean. The third extract was the strongest, and was prepared like the first, except that the proportions differed; so that one minim of it in strength corresponded to four grains of the bean.

With these solutions, I then proceeded to perform the following experiments,—in which I had the able assistance of Dr. Grainger Stewart,—with the intention of elucidating the exact effects the Calabar bean is capable of producing on the eye:—

*Experiment 1.* On the 17th of January, I carefully examined the condition of my eyes, and found that with both my sight was normal. I could see distant objects perfectly distinctly, and could read the finest print (No. 1 of Jaeger), at five inches distance, with either eye. Each pupil measured two lines in diameter, and acted readily under the influence of light. These points having been determined, I introduced a drop of the weakest extract of the Calabar bean into my left eye, at 10 minutes past 12 o'clock. Its introduction occasioned no further irritation than a drop of simple water would produce.

No change was observed in the condition of the eyes until ten minutes thereafter, when, upon looking with the left eye, all objects beyond the distance of about a foot appeared dim and indistinct, but within that distance clear and well defined; while objects at all distances appeared nearer and larger than natural. Vision in the right eye remained unaltered. No difference was visible in the size of either of the pupils. A feeling of straining and heaviness was felt in the left eye similar to that experienced after a prolonged inspection of fine objects near the eye.

At 12:30, or 20 minutes after the introduction of the extract, a marked alteration in the size of the pupils was observable; the left pupil being only 1 line in diameter, while the right measured fully two lines. Looking with the left eye, all objects beyond nine inches from the eye appeared very dim, and at all distances everything seemed about a half larger than natural, and nearer to the eye. Vision in the right eye was unaffected.

At 12:40, the left pupil measured only  $\frac{2}{3}$  of a line, while that of the right eye had dilated to  $2\frac{1}{2}$  lines. The furthest point of distinct vision with the left eye was 8 inches from the eye. In other respects no alteration was observable since last report.

At 1:20, the pupils measured on the left side  $\frac{1}{2}$  a line, on the right 2 lines. With the left eye objects could with some effort be seen distinctly to the distance of about 10 yards, but, as before, larger and darker than with the other eye. When reading with both eyes, a sensation of heaviness and fatigue was soon felt in the left. Vision in the right eye continued unaltered.

At 6 o'clock, the left pupil had dilated to 1 line, while the right had contracted to  $1\frac{3}{4}$  line. Vision with the left was somewhat improved, and with an effort distant objects could be distinctly seen. Both pupils contracted under the influence of light, both singly and sympathetically. At 12 o'clock, the left pupil measured  $1\frac{1}{2}$  line, the right  $2\frac{1}{2}$  lines, and the same symptoms were present as at last report, only to a less marked degree. A dull aching and heaviness was experienced in the left eye consequent upon its exercise in reading and writing.

On the following morning, there was still an appreciable difference in the size of the pupils, and vision with the left eye was still slightly affected; but the symptoms gradually subsided, and in the afternoon completely disappeared.

The results obtained from this experiment were, that the Calabar bean acted first on the accommodation of the eye, causing indistinct vision of distant objects to such an extent that all objects beyond 8 inches from the eye appeared dim and indistinct. The next marked effect produced was contraction of the pupil, its diameter being reduced from 2 lines to  $\frac{1}{2}$  a line. As a natural consequence of less light passing to the retina of the eye experi-

mented on, the pupil of the other eye became sympathetically somewhat dilated, while with the affected eye all objects appeared darker than natural. It is interesting to observe, that while the affection of the accommodation of the eye is the symptom first developed, it also is the first to subside, for we find that while the contraction of the pupil is at its maximum at 1:20, the affection of vision had already decidedly diminished. From the very small size of the pupil it was very difficult to ascertain whether it acted under the influence of light or not. On the occasion of one of the reports (where it is mentioned), it was distinctly observed to do so.

*Experiment 2.* Having ascertained that my eyes had returned to their normal condition, and that each pupil, as before, measured 2 lines, and acted under the influence of light, I again, on January 20th, introduced a drop of the weakest extract of the Calabar bean into my left eye at 8:30 A.M.

At 8:40 the pupils were unaffected. With the left eye objects beyond 9 inches appeared dim, enlarged, and nearer than with the other eye, and a concave glass, of 10 inches negative focus, was required to enable me to see distant objects distinctly. With this concave glass the nearest point at which I could see objects distinctly was 9 inches from the eye.

At 9:05 the left pupil measured  $\frac{3}{4}$  of a line, the right 2 lines. To see distant objects clearly with the left eye, a concave glass of 8 inches negative focus was now required, and with this glass the "near-point" of distinct vision was 5 inches from the eye. Both pupils acted under the influence of light. Vision in the right eye was unaffected.

A drop of a solution of atropine (gr. ij to  $\overline{5}$ i) was now introduced into the left eye.

At 9:30, the left pupil had sensibly increased in size, and measured 1 line, while the right measured  $1\frac{3}{4}$  line. A concave glass of 12 inches negative focus was now sufficient for distinct vision of distant objects with the left eye.

At 10, the left pupil had become dilated to 3 lines, the right pupil remaining unaffected. With the left eye objects beyond 3 feet could alone be distinctly viewed, and all objects appeared

smaller and more distant than natural. The left pupil was insensible to the influence of light. A drop of the extract of Calabar bean, of medium strength, was introduced into the left eye.

At 10:30, all objects beyond 8 inches were clearly seen with the left eye, and the pupils measured 3 lines on the right side and  $1\frac{3}{4}$  line on the left.

Another drop of the same extract of the Calabar bean, as was last employed, was again applied to the left eye.

At 11:30, vision with the left eye was perfectly distinct beyond 9 inches from the eye. There was no alteration in the size of the pupils.

At 1:30, all objects within 12 inches appeared dim and indistinct with the left eye, while everything beyond that distance was clear and well-defined. The left pupil was  $2\frac{3}{4}$  lines in diameter, the right  $1\frac{1}{2}$  line.

Another drop of the extract of the Calabar bean was introduced, which, as before, improved the condition of the accommodation of the eye, the effects lasting about four hours. The application of the Calabar bean was repeated other three times, the effects at each successive application being more marked, and enduring longer. In two or three days, the effects of the atropine and Calabar bean disappeared.

This experiment led me to the conclusion that the Calabar bean and belladonna are exactly antagonistic in their action on the eye; and I ascribed the temporary nature of the improvement effected by the Calabar bean on the eye under the influence of atropine, to the fact that the atropine solution was much stronger than the extract of the Calabar bean I had employed. To put this to the proof I performed the following experiment:—

*Experiment 3.* On February 2d, at 2:10 P.M., I introduced into each of my eyes a drop of a solution of atropine of the strength of gr. ss to  $\mathfrak{z}$ i. By examination, prior to the introduction of the drops, I had ascertained that vision in both was normal—all objects beyond 5 inches from the eye being distinctly perceived—and that the left pupil measured 2 lines, and the right fully  $1\frac{3}{4}$  line in diameter.



At 3:20, the physiological effects of the atropine had manifested themselves pretty decidedly. The right pupil was  $3\frac{3}{4}$  lines, the left  $3\frac{1}{2}$  lines in diameter; the nearest point of distinct vision was—left eye, 8 inches; right eye, 12 inches.

A drop of the strongest extract of the Calabar bean was now introduced into my right eye.

At 3:40, the pupils measured  $3\frac{1}{2}$  lines each. In vision there was a marked difference between the eyes, for with the right eye I could read only very large type (No. 18 of Jaeger, "Canon" type) at 2 feet distance; while with the left, at that distance I could read moderate-sized print (No. 8 of Jaeger, "Small Pica" type).

At 3:55, the state of vision in my right eye was very peculiar. I could only see objects distinctly between  $6\frac{1}{2}$  inches and 9 inches from the eye; anything nearer to the eye than  $6\frac{1}{2}$  inches, or further from it than 9 inches, appearing misty and dim. With the left eye everything appeared distinct beyond 12 inches. The right pupil measured 3 lines, the left  $3\frac{1}{2}$  lines in diameter.

At 4:15, the extent of clear vision with the right eye had very much increased—being in fact almost normal—all objects beyond 6 inches being seen with perfect distinctness. The nearest point of distinct vision in the left eye was 15 inches. There was no alteration in the size of the pupils from last report. Looking with the right eye objects appeared much larger than when viewed with the left. With the right eye I was able to read small print without the slightest inconvenience, while with the left I was unable to read any but large-sized print, and that only held at a considerable distance from the eye.

At 6:55, the effects of the Calabar bean were passing off, the nearest point of clear vision in the right eye being about 18 inches from the eye. Another drop of the strongest extract of the Calabar bean applied to right eye.

At 7:05, distinct vision with the right eye ranged from 6 to 9 inches from the eye; at 7:15 it ranged between  $5\frac{1}{2}$  inches and 8 inches; at 7:55 between 5 inches and 15 inches; and at 8:15, objects at all distances beyond 5 inches could be most clearly defined. Very little alteration was observed in the size of the

pupils or the vision of the left eye. No further application of the Calabar bean was made to the right eye, as the effects of the last application lasted until the effects of the atropine had almost passed off, and exhibited a marked contrast to the left eye, in which the atropine acted uncontrolled.

I have narrated these experiments somewhat in detail, so as to elucidate, as far as possible, the method of action of this new agent and its energy. These experiments prove that the local application of the Calabar bean to the eye induces,—*first*, A condition of short-sightedness. That this is present, and the cause of the indistinctness of distant vision cannot be doubted, as it is relieved by the use of concave glasses. The fact that objects appear larger and nearer than natural may be attributed to the induced myopia. And, *second*, It occasions contraction of the pupil, and sympathetically dilatation of the pupil of the other eye. We further observe that atropine possesses the power of counteracting its effects, and, *vice versa*, that it is capable of overcoming the effects produced by atropine. The first symptom noticed is dimness of distant vision, and shortly after the pupil becomes contracted; the symptoms also subside in the same order, first the derangement of accommodation, and then the affection of the pupil.

Let me now say a few words as to the method of action of the Calabar bean. In respect to its effects on the pupil they might be produced either by causing contraction of the circular fibres of the iris, or by paralyzing its radiating fibres. I am inclined to believe that the contraction of the pupil is due to increased action of the sphincter pupillæ, and this chiefly on the ground that the other effects produced by the Calabar bean can only be explained by an induced contraction of the ciliary muscle—the muscle of accommodation; and as the sphincter pupillæ and ciliary muscle are both supplied by the ciliary nerves, I think the most feasible explanation of the action of the Calabar bean on the eye is to regard it as a stimulant to the ciliary nerves. In favour of this view we have the feeling of straining in the eye shortly after the physiological effects are produced. The alteration, too, in the accommodation of the eye exhibits much of the

character of a spasmodic action; thus we find in experiment *third*, after the second application of the Calabar bean, that the extent of distinct vision is limited to 3 inches, viz., from 6 to 9 inches from the eye, but an hour after distinct vision extends to any distance beyond 5 inches. It has also been observed that the accommodation of the eye is not usually affected in cases where contraction of the pupil is due to lesion of the sympathetic (exemplified in a case narrated by Dr. von Willebrand in the *Archiv. für Ophthalmologie*, vol. i., where contraction of the pupil depended on the pressure of enlarged glands on the cervical sympathetic, and where no affection of the accommodation was present).

As regards the cases in which this substance may be applied in practice, it is applicable in all instances where atropine is used to render the examination of the eye more perfect or more simple. This includes two classes of cases, those in which dilatation of the pupil is either necessary or desirable to aid ophthalmoscopic examination, and those in which paralysis of the ciliary muscle is necessary, in order to ascertain the state of the accommodation of the eye.

In case of retinitis, with photophobia, I think it might be advantageously employed to diminish by contraction of the pupil the access of light to the retina, and this more especially in those cases of this disease where the pupil has been dilated for the purpose of ophthalmic examination.

The cases, however, in which I should expect this remedy to produce the most beneficial effects are those in which paralysis of the ciliary muscles occurs as a consequence of long-continued debilitating disease. Cases of this kind are occasionally reported as following attacks of typhus or other fevers. The dimness of vision that forms a frequent sequela of diphtheria appears also to be due to this cause, judging from the symptoms detailed by Dr. Begbie in an admirable paper on diphtheria, recently published in this Journal; therefore, in these cases, good effects may be expected from the use of the Calabar bean.

In cases of ulceration at the margin of the cornea, leading to perforation, or even when prolapsus of the iris has just occurred,

as well as in cases where the iris has a tendency to protrude through a corneal wound, the contraction of the pupil induced by this agent might prove serviceable by drawing the iris away from the circumference.

I have shortly pointed out the cases in which I consider this remedy may prove useful, but have as yet had but little opportunity to test it practically; I think, however, there can be little doubt that in the Calabar bean we possess an agent that will soon rank as one of the most valuable in the ophthalmic pharmacopoeia.

THE END







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GUIDO BANTI

From Volume VI of *Enciclopedia Italiana*. Kindness of Giovanni Tracani

# MEDICAL CLASSICS

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## Guido Banti

### BIOGRAPHY

- 1852 Born June 8 at Montebicchiere, Italy.  
1877 Age 25. Completed classical studies in Florence.  
1878 Age 26. Assistant in pathologic anatomy in Florence until 1882.  
1883 Age 31. Nominated settore and physician-in-chief in the Hospital of Santa Maria Nuova.  
1887. Age 35. Appointed to teach general pathology in the medical school of Florence.  
1890 Age 38. Made head of Institute of Pathologic Anatomy until 1925.  
1894 Age 42. Described splenomegaly with liver cirrhosis (Banti's disease).  
1896 Age 44. Co-editor of *Revista italiana di patologia generale*, Torino.  
1908 Age 56. Editor of *Pathologica*, 15th revision, Genoa, until 1914.  
1925 Age 73. Died January 8 at Florence, Italy.

### EPONYM

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## INTRODUCTION

Guido Banti became a teacher of pathologic anatomy at the age of 26 and spent the remainder of his life, forty-seven years, in that study. At the age of 27 he began to publish papers on pathology, writing some eighty articles and books before the end of his career. When 30 he wrote a book of seventy pages, *On splenic anemia*, in which he first mentioned a new syndrome, but not until twelve years later, in 1894, did he feel that he knew enough about the condition to write a separate paper on it. He then, having been head of the Institute of Pathologic Anatomy at Florence for four years, described splenomegaly with cirrhosis of the liver, a syndrome with which the name Banti is inseparably connected.

From the first description we find that Banti divided the clinical manifestation into three groups or periods, viz.: preascitic, ascitic and an intermediate period. In a brief and clear manner he discussed the condition as to pathology, possible etiologic factors and differential diagnosis.

Today with our added knowledge of blood diseases and blood examination there is still a lack of agreement on Banti's disease. Many writers advise against using the term, holding that all these cases can be included under other disease titles. W. Boyd (*Surgical Pathology*, Philadelphia, Saunders Co., 1936, p. 579) says, "it is by no means certain that Banti's disease and Laennec's cirrhosis are not merely two different aspects of the same condition." L. M. Rousselot, after studying patients in the Spleen Clinic of the Presbyterian Hospital in New York City, wrote (*Jour. Amer. Med. Assn.*, 107: 1788-1793, November 28, 1936), "As the study developed it became apparent, as it had to many others before us, that we were not dealing with a sequence of clinical and pathological features as described by Banti. Instead we had an apparently heterogeneous group of cases that presented certain similar characteristics and that shall henceforth be grouped under the name of Banti's syndrome." Rousselot is of the same opinion as J. McMichael (*Edinburgh M. J.*, 38: 1, January 1931), believing that a state of portal hypertension, primary or secondary, probably is present in all cases of Banti's syndrome.

Splenectomy, advocated by Banti himself "as the only therapy," has now been performed in numberless cases. J. B. Deaver and S. P. Reimann (*Ann. Surg.*, 88: 355-360, September 1928) strongly advise this operation. But N. Rosenthal (*Jour. Amer. Med. Assn.*, 84: 1887-1891, 1925) and more recently S. W. Moore (*Surg., Gynec. & Obst.*, 63: 382-384, September 1936) have been able to explain some of the poor results following splenectomy by dividing patients into two groups:

(a) A thrombocytopenic group. In these patients the blood platelets are diminished before operation. A transient rise and then a fall to normal or slightly above normal follows splenectomy.

(b) A thrombocythemic group. In this group the blood platelets are normal or below normal before operation but rapidly increase to enormous numbers after splenectomy and remain high permanently. This increase in blood platelets is associated with repeated thromboses and consequent hemorrhages.

In group "a" splenectomy is curative while in group "b" the disease will not be arrested by operation and therefore other forms of therapy, principally radiation, should be employed.

On the following pages the original paper of Banti is reproduced in its original Italian with English translation, followed by a later paper of Banti on the same subject.

# LO SPERIMENTALE

GIORNALE MEDICO

ORGANO DELL'ACCADEMIA MEDICO-FISICA FIORENTINA

DIRETTO DAI PROFESSORI

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STABILIMENTO TIPOGRAFICO FIORENTINO

Via San Gallo, 33

1894



# La Splenomegalia con Cirrosi del Fegato

BY

PROF. G. BANTI

**F**IN. dal 1882 la mia attenzione fu colpita da un complesso sintomatico ed anatomo-patologico tutto speciale, che non è stato, per quanto io ne sappia, descritto fin qui e che potrebbe costituire una novella specie morbosa; voglio parlare della *splenomegalia con cirrosi del fegato*. I casi che vi si riferiscono potrebbero a prima vista esser confusi con la cirrosi epatica del Laënnec, ma tuttavia non è difficile, con un esame accurato, il differenziare le due malattie. Io riferirò più tardi in una memoria completa i fatti osservati; oggi mi limito ad esporre i tratti principali di questa malattia.

## I

Si possono dividere i sintomi in tre stadi: lo stadio *preascitico*, lo stadio *ascitico* e lo stadio *intermedio*.

I sintomi dello stadio *preascitico* sono: la *tumefazione della milza* e l'*anemia*.

La malattia s'inizia con l'*ipertrofia splenica*. Questa si svolge insidiosamente e quando il malato od il medico si occupano delle condizioni anormali della milza, essa ha ordinariamente acquistato un volume considerevole. La milza ipertrofica conserva la sua forma; essa discende di quattro o cinque dita trasverse al di sotto dell'arco costale ed arriva talvolta fino alla cresta iliaca; l'estremità anteriore arriva fino alla linea mediana. Alla palpazione la sua superficie è liscia ed indolente alla pressione. L'iper-

trofia splenica presenta i medesimi caratteri clinici che si ritrovano nella leucocitemia e nell'anemia splenica.

I *sintomi anemici* susseguono alla tumefazione della milza, e consistono, come di consueto, in una debolezza crescente, con pallore della pelle e delle mucose, dispnea e palpitazione al minimo sforzo, ecc. Non si hanno disturbi gastro-intestinali; l'appetito è buono e non v'ha dimagrimento.

I soffi anemici nella regione cardiaca sono costanti. Essi sono sistolici e hanno il loro massimo d'intensità al focolaio d'ascoltazione della polmonare. La diminuzione del numero dei globuli rossi è proporzionale al decorso dell'anemia: in generale se ne contano da 3 a 4,000,000 per millimetro cubo.

Si osserva la poichilocitosi e la microcitemia. I globuli bianchi non sono aumentati di numero e il rapporto fra le diverse specie di leucociti è normale. La quantità d'emoglobina è diminuita ed il valore individuale dei globuli rossi può esser ridotto alla metà (metodo dell'Hayem).

Le urine sono di quantità e di colore normale; esse contengono una quantità normale d'urati e di pigmenti urinari.

Il fegato non presenta alcuna modificazione di volume: è indolente alla pressione; non apparisce alcuna traccia di circolazione venosa supplementare sulle pareti abdominali.

I sintomi anemici possono presentare dei miglioramenti passeggeri, ma non spariscono mai completamente. Nei periodi di miglioramento la milza rimane grossa o diminuisce insensibilmente.

Nei malati che ho avuto occasione di osservare, lo stadio preascitico ha durato un anno almeno e quattro anni e mezzo al più.

Lo stadio *intermedio* è caratterizzato dalla comparsa della dispepsia, di turbamenti intestinali, qualche volta di emorroidi. Nello stesso tempo le urine divengono più scarse, si colorano in rosso carico e si fanno ricche d'urati. Questo stadio dura pochi mesi.

Nello stadio *ascitico* si vede sopraggiungere una raccolta di liquido nella cavità del peritoneo. Il liquido è sieroso, citrino, d'una densità media 1,011 a 1,012. Il fegato si presenta più piccolo che allo stato normale; le urine sono scarse; la loro densità

è da 1,030 a 1,035 e contengono molta quantità di urati e di urobilina. I sintomi anemici divengono più gravi, ma l'esame del sangue fa sempre accertare un numero normale di leucociti. Questo periodo dura da sette a otto mesi e finisce colla morte.

Le *alterazioni anatomo-patologiche* sono le seguenti:

La milza è uniformemente aumentata di volume e può avere un peso di 1 chilogr. ad 1 chilogr. e mezzo. La capsula è ispessita, ma la superficie dell'organo è liscia. L'esame microscopico del succo splenico dimostra l'assenza completa dei globuli rossi nucleati. Su dei pezzi preparati dopo indurimento si nota la sclerosi dei corpuscoli di Malpighi che, a poco a poco, si trasformano in noduli fibrosi. Le vene della polpa splenica sono ristrette. La tessitura reticolare di questa polpa è conservata in più parti, ma i filamenti sono grossi, assumono qualche volta l'aspetto di nastri e presentano un aspetto fibrillare o granuloso. Altrove il tessuto è composto di cellule fusiformi, offrenti l'apparenza di fibroblasti. In altri punti, infine, esiste quasi una trasformazione fibrosa del tessuto splenico.

Il fegato prende i caratteri macroscopici e microscopici della cirrosi atrofica del Laënnec, solamente gli anelli di connettivo sono in generale sottili e presentano una notevole infiltrazione di cellule rotonde.

Il midollo delle ossa, rosso, offre l'aspetto del midollo fetale e contiene un gran numero di globuli rossi nucleati.

L'*etiologia* non offre che notizie negative. Nessuno dei miei malati presentava degli antecedenti ereditari sospetti; si trattava d'individui di buona costituzione, che non erano mai stati affetti da sifilide, da malaria o da altre malattie infettive. Essi abitavano in luoghi salubri; non erano stati esposti a cause d'intossicazione, tenevano un regime alimentare moderato ed alcuni potevano anche passare per vegetariani. In tutti l'abuso del vino o di bevande alcoliche poteva essere escluso in modo assoluto.

## II

Se nell'affezione spleno-epatica che ho tratteggiato, volessimo limitarci a considerare le alterazioni anatomo-patologiche o i sintomi dello stadio ascitico, si sarebbe colpiti della sua



analogia con la cirrosi del Laënnec. Esistono per altro alcuni caratteri ben netti che volgono a differenziarla, cioè:

1. La etiologia della cirrosi del Laënnec manca qui assolutamente;

2. L'anemia progressiva del primo stadio non si riscontra affatto nella sintomatologia delle cirrosi del Laënnec.

3. Nel primo stadio, che può durare perfino quattro anni o quattro anni e mezzo, invano si cercherebbe un segno di malattia del fegato. Quest'organo ha un volume normale; è indolente; non si hanno disturbi gastro-intestinali; le urine sono abbondanti e contengono una quantità normale di urati e di pigmenti urinari, ecc.

4. L'ipertrofia splenica è il primo sintoma che si manifesta. Se esso dipendesse dalla stasi venosa, come si giungerebbe ad intendere che una malattia epatica, arrivata al punto da ostacolare sì gravemente la circolazione della vena porta, possa restare tre o quattro anni senza dar luogo ad altri sintomi?

5. Le lesioni istologiche della milza, prodotte dalla stasi, sono assai differenti da quelle che io ho osservate nella splenomegalia con cirrosi. L'ipertrofia da stasi è dovuta principalmente alla distensione delle vene, ed un po' all'ispessimento del tessuto fibroso (Cornil e Ranvier). Nella splenomegalia le vene spleniche sono ristrette e le trabecole del tessuto reticolare sono assai ispessite (*fibro-adenia*).

Questi caratteri mi sembrano sufficienti per distinguere la splenomegalia con cirrosi epatica dalla cirrosi del Laënnec. Io credo dunque che nella malattia che io descrivo le alterazioni del fegato rappresentino l'ultima fase d'un processo, il cui principio è segnato dai sintomi dello stadio intermedio.

La splenomegalia con cirrosi ha piuttosto delle analogie con l'anemia splenica. Per lo studio dell'anemia splenica, io rinvio il lettore alla monografia che già pubblicai nel 1883,<sup>1</sup> nella quale, appoggiandomi sopra osservazioni personali, trattai per la prima volta in modo completo la sintomatologia e l'anatomia patologica

<sup>1</sup> G. BANTI, *Dell'anemia splenica* (Archivio della Scuola d'Anat. Pat., vol. II, Firenze, 1883.)

di questa malattia. Al presente mi limito a dichiarare che i sintomi dell'anemia splenica sono assolutamente identici a quelli della splenomegalia nello stadio preascitico, nè io saprei indicare un segno differenziale fra queste due affezioni.

I sintomi del secondo e del terzo stadio della splenomegalia sembrano al contrario indicare una differenza netta fra questo stato morboso e l'anemia splenica. Ma le differenze scompaiono in parte se si considerano le alterazioni istologiche della milza e del fegato che caratterizzano queste due malattie.

Nell'anemia splenica si trova nella milza una sclerosi dei corpuscoli di Malpighi e una fibro-adenia della polpa; queste lesioni differiscono dalle lesioni proprie alla splenomegalia unicamente per la loro minore intensità.

Nel fegato si osserva una infiltrazione di leucociti negli spazi triangolari e nelle fessure, qualche volta pure un leggerissimo aumento del tessuto connettivo interlobulare. Si direbbe che nell'anemia splenica esiste un abbozzo di cirrosi, mentre nella splenomegalia si ha una cirrosi confermata.

È per questa ragione che si potrebbe essere spinti a considerare la splenomegalia con cirrosi, non come una entità morbosa, ma piuttosto come uno stadio più avanzato dell'anemia splenica.

Una discussione a questo proposito sarebbe, io credo, del tutto sterile. Ci esporremmo a facili errori se volessimo affermare o negare l'identità di due malattie basandosi solamente sui sintomi o sulle alterazioni anatomiche. Forse la tubercolosi miliare e la febbre tifoide non possono presentare una sintomatologia identica? Lo stafilococco aureo e il bacillo dell'Eberth non possono ambedue produrre un ascesso? Per differenziare o identificare in maniera scientifica due forme morbose, bisogna fondarsi sulle cause e queste ci sono sconosciute tanto nell'anemia splenica come nella splenomegalia con cirrosi.

Però se quest'ultima non fosse che uno stadio finale dell'anemia splenica, bisognerebbe stupirsi che tale stadio si raggiungesse così raramente e che anche nei casi di anemia, che sono durati due anni e più, il fegato non presentasse ancora i segni di una cirrosi manifesta.

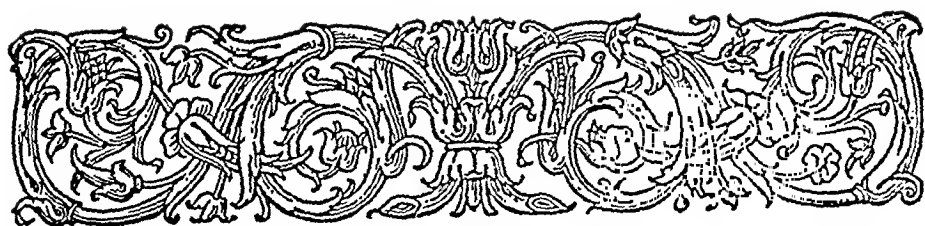
## III.

Sarebbe prematuro oggi l'espore una dottrina che valesse a spiegare lo sviluppo della splenomegalia con cirrosi. L'ipotesi alla quale io preferirei tenermi sarebbe la seguente:

Forse la malattia sarà di natura infettiva: comunque, le cause morbose porterebbero fin da principio la loro azione sulla milza. In quest'organo si formerebbero, sia in virtù di processi biochimici anormali, sia in seguito alla presenza di un agente infettivo, delle sostanze tossiche che penetrerebbero nel sangue e determinerebbero così un'anemia progressiva. Queste stesse sostanze traversando incessantemente il fegato, potrebbero causare una irritazione analoga a quella dell'alcool e la cirrosi ne sarebbe la conseguenza ultima.

Io proponeva questa spiegazione nel 1882 per l'anemia splenica ed in suo appoggio posso allegare certi casi di estirpazione della milza (Spencer Wells, Péan, Czerny, Franzolini, ecc.) seguiti dalla guarigione completa dell'anemia.

Che che si pensi di questa interpretazione, io stimo che *la splenomegalia con cirrosi epatica* rappresenti un'entità morbosa che merita di richiamare l'attenzione dei medici. (Dalla *Semaine Médicale*, 11 juillet 1894.)



# Splenomegaly with Cirrhosis of the Liver

BY

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(This is a translation of the paper, *La Splénomégalie avec cirrhose du foie*, in *Semaine Méd.*, Paris, 14: 318, 1894 which in turn is a translation of the original paper in Italian, *La Splénomégalia con cirrosi del fegato*, in *Sperimentale*, Firenze, 1894, *Comun. e Riv.*, 447-452 and *Sez. Biol.*, 48: 407-432).

**I**N 1882, my attention was directed to the existence of a symptomatic and anatomo-pathological complex which, so far as I am aware, has never been described, and which may well be considered as a special kind of disease, namely, splenomegaly with cirrhosis of the liver. Cases of this disorder may easily be confounded at first sight with Laennec's hepatic cirrhosis, but a careful examination shows clearly that there is a difference between the two. Later on I shall discuss these cases in a special monograph; for the present I will confine myself to a sketch of the principal characteristics of this disease.

## I

The symptoms of the disease may be divided into three groups, corresponding to as many periods, viz.: the pre-ascitic stage, the ascitic stage, and an intermediate stage.

The symptoms of the pre-ascitic stage are: tumefaction of the spleen and anemia.

The disease sets in with splenic hypertrophy, which progresses in an insidious manner, so that when it is noticed by the patient or his physician, the spleen has usually attained a considerable size. The spleen, though hypertrophied, retains its normal shape; it descends four or five fingers' breadth below the last costal arch and sometimes as far as the iliac crest; its anterior border frequently reaches the median line. Its surface is smooth on palpation and gives no sign of tenderness on pressure. The hypertrophy of the spleen, consequently, presents the same clinical characters as are found in leucocythaemia and splenic anaemia.

Anaemic symptoms follow upon tumefaction of the spleen and consist, as a rule, in increasing debility, with pallor of the skin and mucous surfaces, dyspnoea and palpitation consequent upon the slightest effort, etc. No gastrointestinal disturbances; appetite good and no emaciation.

Anaemic murmurs are constantly present in the cardiac region. They are systolic and their maximum intensity is found in the auscultation area of the pulmonary orifice. The diminution in the number of red blood-corpuscles is proportional to the intensity of the anaemia; usually there are from 3 to 4 millions in a cubic millimetre. There is poikilocytosis and microcythaemia. The white blood-corpuscles are not increased numerically, and the ratio between the different species of leucocytes is normal. The quantity of haemoglobin is decreased, and the individual value of the red corpuscles may be reduced to one-half (Hayem's method).

The liver presents no modification in size, and is not tender to pressure. There is no trace whatever of collateral venous circulation on the abdominal walls.

The anaemic symptoms are subject to temporary amelioration, but never disappear entirely. During these periods of amelioration, the spleen remains as large as before, or at best the diminution in size is so small as to be barely perceptible. In the cases with which I have had to deal, the pre-ascitic stage varied in duration from one year to four years and a half.

The intermediate stage is characterized by the appearance of dyspnea, intestinal disorders, and sometimes haemorrhoids. At the same time the urine grows scantier, dark-red in colour, and rich in urates. This stage lasts a few months.

In the ascitic stage a liquid effusion takes place into the peritoneum. This liquid is serous, lemon-coloured, and its average specific gravity is 1,011 or 1,012. The liver appears to be smaller than under normal conditions; the urine is scanty, with density of from 1,030 to 1,035, and contains a great deal of urates and urobilin. The anaemic symptoms become more and more marked; but the examination of the blood continues to give evidence of a normal number of leucocytes. This stage lasts from seven to eight months and ends in death.

The anatomico-pathological changes are the following:

The spleen is uniformly enlarged in size and may weigh as much as 1 or  $1\frac{1}{2}$  kg. The capsule is thickened, but the surface of the organ is smooth. Microscopical examination of the splenic juice shows complete absence of nucleated red corpuscles. In specimens prepared by hardening, the Malpighian corpuscles are found to be sclerotic, being gradually transformed into connective-tissue nodules. The veins of the splenic pulp are contracted. The reticulate texture of the pulp is preserved at several points, but its filaments are large and sometimes take the form of tapes, presenting a fibrillary or granular aspect. In places, the tissue is composed of fusiform cells, resembling fibroblasts in appearance. At other points of the spleen a fibrous change of the splenic tissue has taken place. The liver presents macroscopical and microscopical characteristics of Laennec's atrophic cirrhosis, with the exception that the connective-tissue rings are, in general, very small and show marked infiltration of round cells.

The bone marrow is red, presenting the appearance of foetal marrow, and contains a large number of nucleated red blood-corpuscles.

The aetiology has nothing to offer us but negative information. None of my patients had a history that was in the least suspicious. They were endowed with a good constitution, and had never suffered from syphilis, malaria, or other infectious diseases.

They lived in healthy localities, were not exposed to infection, were not heavy eaters, and some even might be described as vegetarians. In not a single case was there any evidence of intemperance in the use of wine or alcoholic drinks.

## II

If, in the spleno-hepatic affection described, we only consider its anatomo-pathological lesions or the symptoms of the ascitic stage, its resemblance to Laennec's cirrhosis is very striking. There exist, however, clearly marked differential characteristics, viz.:

(1) The aetiology of Laennec's cirrhosis is entirely absent in this case;

(2) The progressive anaemia of the first stage is not met with among the groups of symptoms of Laennec's cirrhosis;

(3) In the first stage, which may last for from four to four and one-half years, no trace of affection of the liver is discoverable, this organ being normal in size with no pain or tenderness; there are no gastro-intestinal troubles; the urine is abundant and contains a normal quantity of urates and urinary pigments;

(4) Hypertrophy of the spleen is the first symptoms noticed. If it were due to venous stasis, how could the circumstance be accounted for, that an hepatic affection, of sufficient intensity to seriously impede the circulation of the portal vein, has existed for three or four years without determining other symptoms?

(5) The histological lesions of the spleen, produced by stasis, differ widely from those which I have observed in splenomegaly with cirrhosis. Hypertrophy by stasis is due principally to distention of the veins, and a little to thickening of the fibrous meshes (Cornil and Ranvier). In splenomegaly the splenic veins are constricted and the trabeculae of the reticulate tissue are greatly thickened (fibro-adenia).

These distinctions seem to me to be sufficient for separating splenomegaly with hepatic cirrhosis from Laennec's cirrhosis. I am of opinion, that the changes in the liver represent the final stage in a process, the beginning of which is marked by the symptoms of the intermediate stage.

Splenomegaly with hepatic cirrhosis is rather, in fact, related to splenic anaemia. For the study of the latter I would refer the reader to the monograph which I published in 1883,\* and in which the symptomatology and pathological anatomy of this disease were treated in a complete manner for the first time. I will merely say at present that the symptoms of splenic anaemia are absolutely the same as those of splenomegaly in the first stage, and I know of no differential sign between these two affections.

The symptoms of the second and third stages of splenomegaly, however, seem to point to an essential difference between this morbid condition and splenic anaemia; but the difference vanishes if we take into consideration the histological changes of the spleen and liver, which characterize both diseases.

In splenic anaemia the spleen presents sclerosis of the Malpighian corpuscles and fibro-adenia, these lesions differing from those of splenomegaly in that they are less intense. In the liver there is infiltration of leucocytes into the triangular spaces and the fissures, sometimes also slight increase of the inter-lobular connective tissue. One might say that in splenic anaemia the cirrhosis is merely outlined, while in splenomegaly it is fully developed.

For this reason, splenomegaly with hepatic cirrhosis ought to be looked upon, not as forming a separate morbid entity, but rather as a more advanced stage of splenic anaemia.

It would be useless, it seems to me, to attempt to determine whether such a view is, or is not, correct, inasmuch as it is impossible to either affirm or deny the identity of two diseases on the ground of their symptoms or anatomical changes. Do not for instance, miliary tuberculosis and typhoid fever sometimes present an absolutely identical symptomatology? May not both the staphylococcus aureus and Eberth's bacillus produce an abscess? In order to differentiate or identify two morbid conditions with strict regard to scientific principles, we must know the determining causes of both, and of these we know nothing.

\* G. Banti. Dell' anemia splenica. (Archivio della Società di Medicina, 1883, II, Florence, 1883.)



either in respect of splenic anaemia or splenomegaly with cirrhosis.

Nevertheless, supposing that the latter were only the final stage of splenic anaemia, it would be astonishing, indeed, that this stage is so rarely reached, and that even in cases of splenic anaemia which have lasted for two years or more, the liver does not present clearly marked symptoms of cirrhosis.

### III.

It would be premature to attempt to construct at the present time a theory capable of explaining satisfactorily the development of splenomegaly with hepatic cirrhosis. I venture, however, to suggest the following considerations on this subject:

It may be that the disease is of infective nature; in any case, the morbid causes exert at once their action on the spleen. In this organ may originate, either through an abnormal biochemical process, or in the presence of an infective agent, toxic substances, which penetrate into the blood and thus determine progressive anaemia. These substances, constantly passing through the liver, may there determine an irritation, similar to that caused by alcohol, of which cirrhosis is the final outcome.

I suggested this explanation in 1882 with regard to splenic anaemia, and it has since been confirmed by several cases of extirpation of the spleen (Spencer Wells, Péan, Czerny, Franzolini, etc., etc.), which was attended with complete recovery from the anaemia.

Be the explanation what it may, I think splenomegaly with hepatic cirrhosis is a disease well worthy of the serious attention of the medical profession.



# Splenomegalie mit Lebercirrhose (Splenomegaly with Cirrhosis of the Liver)\*

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**I**N 1894<sup>1</sup> I noted a new type of disease, never before observed, and described it as to its clinical and anatomic behavior. Since publication of that description other cases have appeared in the literature, some under the same name, splenomegaly with cirrhosis of the liver, and some as "Banti's disease." They were observed in Italy and France and have been described by Prof. Silva, Dr. Cavazzani, Prof. Galvagni and Dr. Guicciardi, Dr. Bonardi, Dr. Ascoli, Dr. Rinaldi, Dr. Roque and Bett. I myself have observed other cases which add much to our knowledge of this disease as to its clinical behavior, pathological anatomy and therapy; these cases are to be published shortly. In the present study the chief data are to be given as briefly as possible.

*Etiology.* The disease develops chiefly in young people and adults and its causes are entirely unknown. Malaria, syphilis and infectious diseases of various kinds are excluded completely, and the same is true of acute or chronic poisoning, errors in diet,

\* This paper was translated in the Department of Literary Research of the American College of Surgeons. E. C. K.

<sup>1</sup> Sem. médicale, July 11, 1894. Lo Sperimentale, Sez. biologica, 48, 1894.

digestive disturbances, alcoholism, etc. Many of the patients had always enjoyed good health previously while some had had diseases which were in no way connected with the one described here. In no instance were there a number of cases in one and the same family or group of dwellings.

*Symptomatology.* The symptoms may be divided into three stages:

- 1) The anemic,
- 2) A transitional stage,
- 3) The ascitic stage.

First there is an enlargement of the spleen which develops slowly and insidiously, so that the patients notice it only by accident or leave it to be discovered by the physician later. In a few cases, however, it has been determined with certainty that this symptom precedes all others. The splenic tumor achieves considerable volume, much like the leukemic spleens. The spleen has a smooth surface and rounded edges; it is hard, movable in connection with respiration and almost always free from pain unless there is perisplenitis, which is rare.

Following the splenic tumor we find the symptoms of anemia; at first they are light and then gradually become more severe. The common ones are: ready fatigue, palpitation of the heart and respiratory difficulty in connection with exertion, pallor of the skin and mucous membranes, dyscratic cardiac sounds, etc. Frequently there is nose bleeding. Later one often finds edema of the feet, a symptom which disappears when the patient lies quietly.

The blood shows reduction of red corpuscles and hemoglobin to a degree corresponding to anemia. One can determine poikilocytosis and microcythemia; the blood corpuscles containing nuclei are always absent. Leucocytes are present in normal quantities, there is no leucocytosis, and the relation between the different types of leucocytes is normal. The urine is also normal both as to quantity and color. It contains neither albumin, glucose, urobilin, nor gall pigments; the urates are found in normal quantity. In only a few cases slight albuminuria has been observed. The liver is normal; in the last stages of the anemic period it may seem somewhat enlarged.

Ascities is completely absent. The digestive functions usually remain normal and the appetite usually is good. There is no trace of swelling of the lymph glands. The temperature remains regular during the early part of the course, but there are relatively frequent attacks of fever with chills which occur at long, uneven intervals. In one patient whom I observed during such attacks, the volume of the spleen was reduced during the time the fever lasted only to return to its former size as soon as the temperature returned to normal. In some cases the temperature rises every evening during the further anemic period.

The anemic stage is of rather long duration, usually 3 to 5 years, but may also last for 10 or 11 years. The usual anemic symptoms show changes for the better or worse, improving usually after treatment with arsenic. But even during the periods of improvement the splenic tumor does not disappear.

In the transitional stage the characteristics of the urine change. The quantity decreases, it contains generous urates, urobilin, and frequently traces of gall pigments. The skin and the conjunctiva of the patient take on an icteric coloring. The gastric and intestinal functions are disturbed. This stage lasts for only a few months.

The ascitic stage begins with the formation of ascites which takes place slowly and painlessly. The liver decreases in size; the spleen retains its usual characteristics. The scanty urine contains large quantities of urates, urobilin, and bilirubin. The yellow coloring of the skin and the conjunctiva increases, but the feces always remain dark in color. The ascitic liquid is citron-yellow, transparent, and has the characteristics of transudates. There was only one case in which there was chylous ascites (Bonardi), but in this case the disease was connected with insufficiency of a mitral valve. All of the symptoms of anemia become exacerbated and in the evening there is often elevation of temperature. Blood examination shows increasing reduction of the red corpuscles and the hemoglobin; there is no increase in the white corpuscles. Death usually takes place at the end of 5 to 7 months; this stage rarely lasts more than a year.

*Pathological Anatomy.* The actual lesions of the disease are

found in the abdominal cavity; the thoracic and nervous organs, etc. are healthy unless complications set in.

The spleen has an abnormally large volume and a weight of from 1 to  $1\frac{1}{2}$  kg. It retains its normal shape, the surface is smooth and regular, the capsule is often dull and thickened, but adhesions with the adjoining organs are not frequent. The parenchyma is tough and dark red in section; on the brown background one can see whitish stripes, corresponding to the "sepi-ments" which have been cut through in various directions; often one also finds round, whitish, hard nodules which correspond to the Malpighian bodies.

In the ascitic stage the liver is reduced in size, granulated, hard and shows all the characteristics of Laennec's atrophic cirrhosis. In the transitional stage the liver may still have normal volume and a smooth or slightly granulated surface. I have never had the opportunity of performing an autopsy in the anemic stage, but in cases in which splenectomy has been performed during this stage the liver was completely normal in appearance.—In the ascitic stage there is free serous accumulation in the abdominal cavity; in the two preceding stages this symptom is not present.

The portal vein with its ramifications is distended in the ascitic stage but in the transitional stage it is normal. In all cases in which I had a chance to perform an examination with this in mind, I found the intima of the splenic vein and the portal vein, from the orifice of the splenic vein to the liver, covered with rigid, raised platelets which might be diffuse or circumscribed and showed all the characteristics of the atheromatous and sclerotic plates of the aorta. In the transitional stage these thickenings were confined to the veins mentioned while the other branches which emptied into the portal vein were normal; in the ascitic stage they extended also to these branches but in lesser degree.

The lymph glands in the various parts of the body are healthy. The gastro-intestinal tract is normal in the second stage, in the third one finds the same well-known lesions as in atrophic cirrhosis of the liver, but in lesser degree. Particularly slight are

the thickening of the intestinal walls, the clouding of the peritoneum, and the shortening of the small intestine. The bone marrow, including that of the long bones, is reddish, like the lymphoid or the fetal.

Microscopic examination of the splenic juice shows that the nucleated red blood corpuscles are absent completely and that the cells containing blood corpuscles are very rare.

For purposes of examination the spleen was hardened in alcohol, in sublimate, in Muller's, and in Foa's fluids. The results of histological examination are as follows:

The splenic capsule is usually thickened and consists of thick bundles of connective tissue with parallel course; the trabeculae which branch from the capsule into the parenchyma as well as those which enter from the hilus with the vessels, are thicker but otherwise show normal structure.

There were several Malpighian bodies which were of normal appearance under low as well as high magnification. In others low magnification showed that only the periphery consisted of the usual cellular elements whereas there was a zone of greater or less width around the arteries, which occupied  $\frac{1}{3}$ ,  $\frac{2}{3}$ , or  $\frac{3}{4}$  or even more of the diameter of the body, and seemed to be composed of connective tissue with sparse cell nuclei. Under higher magnification it was found that this inner portion actually consisted of dense, hardly fibrous, and almost hyaline connective tissue, in which there were clefts or small meshes which varied in form but usually were spindle-shaped and oval with their longitudinal axis lying concentric to the artery of the body. A few of these alveoli were empty, in others it was found that one or two round or oblong nuclei, rich in chromatin, were attached to a point in the wall; these nuclei showed diffuse susceptibility to stain and showed no distinct supporting structure of threads. A few nuclei were flattened, others were irregular in shape and had shriveled; some had only sparse chromatin and had a blister-like appearance. The diameters of these nuclei varied from 3 to 6  $\mu$ ; the flattened ones had a maximum width of about 1.5  $\mu$ , and a length of approximately 6 to 8  $\mu$ . A few similar nuclei were distributed here and there in the broad trabeculae of connective

tissue which bounded the alveoli. The nearer one approached the periphery of the body, the wider did the alveoli become and the greater was the number of cells which they contained. The trabeculae become constantly thinner and finally formed a coarse net-work which reminded one somewhat of normal reticulum but it differed from the latter in its strength and the hyaline appearance of its fibers. The elements enclosed in the meshes of this net-work were similar in volume and appearance to the normal elements of the external zone of the small body. The artery of it lay always in the sclerotic portion of the Malpighian body and its walls were completely transformed into fibrous tissue.

The sclerotic zone increases in size as the disease progresses. In certain cases one also finds completely fibrous nodules which are readily recognized as sclerotic Malpighian bodies.

If we observe the Malpighian bodies in which the lesions are still in the beginning stage, and particularly if the patient is still in the anemic or the transitional stage, we find that the lesions begin around the artery. As a matter of fact, in some bodies with eccentric artery one can sometimes observe that the lesions begin around the artery in the portion immediately outside the Malpighian body. This fact is noted also in the advanced periods, in which one may observe fibrous shoots; these shoots emanate from wholly or partially hardened bodies and lose themselves in the pulp of the spleen. In many instances one can also observe large sclerotic trunks which divide into a number of branches, with these branches terminating in various bodies. The extent of the sclerosis in the bodies is not uniform; in the beginning it may be confined mostly to one segment, leaving the other portions untouched.

Formation of the sclerotic tissue occurs by way of thickening of the reticulum of the body. The fibers gradually grow thicker, take on a hyaline appearance, and the cellular elements become more rare. In this manner, increasing imperceptibly, the sclerotic tissue enclosing the meshes develops. In the course of this process one observes no karyokinesis, either in the cells of the body or in the actual reticular cells.

Also in cases of advanced disease a portion of the Malpighian

bodies seem to be normal, in others one readily finds the various stages of fibrous transformation.

In two cases, one of which was in the anemic while the other was in the transitional stage of the disease, I also found other lesions in the bodies. In the middle of some of them one could see large hyaline lumps which varied in size, form, and appearance. Some were similar in type and hyaline, others were irregular in shape and seemed to develop by way of accumulation of small bodies; some were round, others angular, still others irregularly elongated and ramified. Because of the frequent irregularities in form their volume was determinable only by measuring many diameters of one and the same body; measurements varied between 10, 20, 50 and 80  $\mu$  and often more. These lumps were resistant to the action of acetic acid; with eosin and the van Gieson mixture they were stained a rosy color. Under nuclear stains they took on a weaker (paler), diffuse color; they did not react like amyloid substances. With nuclear staining, however, one could determine that some of them had round and oval nuclei which had taken on a very pale stain. Between these hyaline formations there were always cells with nuclei showing very weak staining or none at all.

I have not succeeded in explaining completely the origin of these hyaline formations. They were usually found in the bodies having an epitheloid center and around them there were always a few cells with signs of hyaline necrosis. In addition these Malpighian bodies showed two other noteworthy conditions: 1) thrombosis of various vessels, and 2) a peculiar change of the reticulum. The fibers of it were not uniformly thickened; they had a varicose appearance and irregular contours, with thickened places and strictures alternating. I therefore suspect that the hyaline lumps developed from fusion of necrotic cells and from fragments of this reticulum; a few might be fragments of hyaline thrombi. But I am unable to say what these formations mean, i.e. whether they are an accidental manifestation and perhaps have some connection with vascular thrombosis, or whether they are a stage of the histo-pathological process which is running its course in the spleen.



As to the changes in the pulp of the spleen, it should be noted that its venous system does not show distension of the individual vessels either in the anemic, the intermediary, or the ascitic stage.

In the first stages one can notice, in circumscribed portions of the splenic pulp, that the inner surface of some of the veins has a lining of large cells, so that the vessel looks almost like an epithelial canal in cross section. These multiangular or flattened cells have a sparse protoplasm and a rather large nucleus ( $5-8\ \mu$ ). The nuclei, which are usually irregularly oval in shape with their membranes showing notches or depressions, have a very slight chromatic content and often have a blister-like appearance. In the reticulum surrounding the vein one also sees cells of similar character. In some of the veins a number of these cells detached from the wall fill the vessel, so that it presents almost the appearance of cancer alveolus. Cells with karyokinetic nuclei are very rare, so that one hardly finds one.

In a few of the veins one can occasionally find an actual multinuclear giant cell, also rare cells which contain normal blood corpuscles or fragments of such.

The reticulum of the pulp has distinctly thickened fibers of hyaline appearance. In all cases in which I had an opportunity of making a microscopic examination (all individuals who had been ill for a number of years), this thickening was very noticeable. After staining according to Ribbert's method the contrast between this and the normal spleen was very striking; the reticulum was coarse and the meshes were much smaller. The cells contained in the reticulum were perhaps less numerous than in normal spleens but in their various characteristics they showed no changes worthy of note.

The thickening of the reticulum becomes more and more marked as the disease progresses and finally there may be a fibrous transformation of individual regions of the splenic parenchyma. In the places so changed one finds fibrous bundles of connective tissue in parallel course, and between them small clefts and apertures in which a few cellular elements have collected. Between the bundles of fibers there are large oval nuclei with sparse quantities of chromatin.

In the cells within the reticulum of the pulp, as well as in those which lie upon the reticulum itself, one very rarely finds manifestations of karyokinesis. Cells with blood pigment are also very rare.

Therefore the essential changes in the Malpighian bodies as well as in the splenic pulp consist of marked thickening of the reticulum. But the peculiar net-like structure of the adenoid tissue persists except in a few places where complete sclerosis has set in. For this reason I have, since 1882, applied the term "fibroadenia" to such lesions.

The mechanism of thickening of the reticular fibers is not distinctly evident. Certainly one can not attribute it to neoformation of connective tissue in the usual sense of the word because there is no sign of hyperplasia in the splenic cells. It seems almost as though the reticulum becomes thickened by excretion of previously existing cells and this might have some connection with the theory according to which the fibrous intercellular substance of the connective tissue does not develop by direct transformation of the fibroblasts but originates in excretion from the fibroblasts.

In the liver there is a ring-shaped interlobular cirrhosis similar to the alcoholic type. It begins, therefore, in the interlobular spaces around the ramifications of the portal vein and then extends into the interlobular clefts. Even in the advanced periods of the disease I have never found this cirrhosis to develop the intensity of the alcoholic type. The rings of connective tissue are rather thin and they are usually permeated by a number of small round elements which look like leucocytes. In the transitional stage of the disease, the hyperplasia of the connective tissue is in a state of origin.

In the splenic vein we find the lesions of sclerotic endophlebitis. The intima showed non-uniform thickening. It consisted of thick bundles of fibers which were slightly fibrinous or showed hyaline poverty as to cells. One can also find actual atheromatous or calcified foci. Such changes continue into the portal vein, beginning at the mouth of the splenic vein. In the other ramifications opening into the portal vein, I was unable to find any changes in a woman who died during the transitional stage.

During the ascitic stage the mesenteric veins may also show lesions but these are much less marked than those in the splenic veins.

The bone marrow has fetal characteristics but the supply of nucleated red blood corpuscles is usually not large.

*Bacteriological Examination.* I have examined the following:

- 1) Venous blood, taken from the living,
- 2) Splenic juice, drawn from the living during attacks of fever,
- 3) Splenic juice from a spleen just extirpated by a surgeon,
- 4) Spleen of cadavers.

Cultures were made in meat broth, in gelatine, in agar-agar, in glycerine-agar, in liquid and coagulated blood serum, in pleuritic serum, and in ascitic serum. Both aerobic and anaerobic cultures were made. In no instance did the author achieve development of microorganisms.—Microscopic examination of the blood, the splenic juice, and the spleen hardened in alcohol did not reveal the presence of bacteria or of malaria parasites. The same negative findings have been made also by other observers (Silva, Bonardi, Rinaldi).

In order to make the characteristics of this disease even more striking, I should like to call attention to the fact that it defines all medical measures except arsenic preparations, which bring temporary improvement. The disease progresses slowly but it inexorably drags the patient to his death.

In three cases Prof. F. Colzi of the surgical clinic in Florence performed splenectomy. One of the patients died of a puerperal complication independent of the operation, several days after intervention. One young man recovered completely, the symptoms of anemia disappeared rapidly, and at the time of writing, 33 months after operation, was in the best of health. In his case operation was performed in the anemic stage, after an illness of approximately 6 years.

Another woman was operated upon after 7 or 8 years of the disease. In operation the liver was found to be somewhat granulated at the surface, showing that cirrhosis of the liver had already set in. The woman recovered completely; now, at the end of 21 months, no more anemic symptoms or other manifestations of hepatic disease are determinable.

The disease picture just described has nothing in common with Laennec's cirrhosis of the liver, from which it differs in its negative etiology, its long first stage of anemia, the splenic tumor which precedes the cirrhosis by a number of years, etc. In its first stage it is similar rather to another disease, namely splenic anemia.

The first case of progressive anemia observed in connection with a large tumor of the spleen was described by Woillez<sup>2</sup> in 1856. Gretsche<sup>3</sup>, who reported on a similar case in 1867, was the first to use the term "splenic anemia." A few isolated cases have been reported by Muller,<sup>4</sup> Pye-Smith,<sup>5</sup> Lidi,<sup>6</sup> and others, but not always under the same name. The much-quoted case of Strumpell<sup>7</sup> should be classed as pernicious anemia and not as splenic, because autopsy showed that the spleen was normal as to volume and structure. In 1882<sup>8</sup> I collected a few cases scattered about in the literature, and basing my views chiefly on my own observations, I presented the first clinical description of this disease. I discussed the anatomic and the macro- and microscopic changes and proposed a pathogenic explanation. Since that time new cases have been published, but nothing new has been added to illuminate the picture further.

The chief clinical characteristics of splenic anemia in adults are; the marked enlargement of the spleen and the increasing and fatal anemia. The anatomic changes are located in the spleen and correspond to those of the disease picture described here; in the liver there are deteriorations of the parenchyma cells and occasionally also a rather slight hyperplasia of the interlobular connective tissue. Death is induced by cachexia.

I cannot agree with Stumpell when he says that "no definite line can be drawn between such cases (of splenic anemia) and the more severe forms of essential anemia with moderate enlargement of the spleen."—Enlargement of the spleen in the severe

<sup>2</sup> Bull. de la Soc. méd. des hôpit. 1856.

<sup>3</sup> Berl. klin. Wochenschr. 1867.

<sup>4</sup> Berl. klin. Wochenschr. 1867.

<sup>5</sup> The Lancet 1875.

<sup>6</sup> Contributo allo studio della leucocitemia, linfoma maligno ecc., Bologna 1880.

<sup>7</sup> Archiv der Heilkunde 1875 u. 1877.

<sup>8</sup> Dell'anemia splenica, Firenze 1882.

forms of essential anemia is due either to a return of the hemopoietic function or to an increased disintegration of the red blood corpuscles; in splenic anemia of adults it is connected with important structural changes in the reticulum (fibroadenia). These lesions are similar to those of spleno-lymphatic pseudo-leucaemia. The cases of Woillez, Gretschel, Concato,<sup>9</sup> etc. show that in splenic anemia the patient may, in addition to tumor of the spleen, develop hypertrophy of some of the lymph glands or of several groups of these glands. We may therefore assume that splenic anemia may be looked upon as a pure "pseudoleucaemia splenica."

It is undeniably true that, in the anemic stage, splenomegalia with cirrhosis of the liver is similar to splenic anemia; we might therefore think that it is only a more advanced stage of it.

I admit the possibility of this hypothesis but I do not think it can be proved either in the affirmative or the negative. The only noteworthy mark of differentiation, on the basis of which one might recognize the similarity or difference of the diseases, is the etiology; the similarities between the symptoms and the anatomic lesions found in the two diseases are inadequate and unscientific ear-marks. A similar problem is found in cerebro-spinal meningitis, the symptoms of which are the same while its nature is quite different, depending on whether it is caused by the *Diplococcus intracellularis* or the *Diplococcus lanceolatus*. Since the causes of splenomegalia with cirrhosis of the liver and of splenic anemia are totally unknown there is no point in discussing the relation between the two. I wish only to make the following statements:

1. In splenic anemia, even that of long duration, there is no macroscopically determinable cirrhosis of the liver; in the disease here described, however, it is always present even after a much shorter course.
2. In a few cases of splenic anemia hypertrophic lymph glands were found, proving its kin-ship with pseudoleucaemia; in splenomegalia with cirrhosis of the liver nothing of the sort has been observed.

<sup>9</sup> Giorn. internaz. delle Scienze mediche 1881.

3. In splenic anemia of children, which is very similar to that of adults, hyperplasia of the connective tissue in the liver is absent.

Of course I must leave the question undecided.

With reference to the pathogenetic explanation of splenomegaly with cirrhosis of the liver, I think I am justified in saying the following:

The first symptom in chronological order is tumor of the spleen and this is followed by anemia; many clinical reports make specific statements on this point. The anemia is a direct result of the splenomegalia. This statement is supported by the clinical processes and also by "experiment" in man, because splenectomy has led to rapid and complete recovery from anemia, even when this operation has been performed in advanced stages of the disease.

How does anemia develop from affection of the spleen? It is certainly not because the spleen discontinues its blood forming function; we know now that in adults such function emanates only from the bone marrow. We can not assume either that there is excessive destruction of red blood corpuscles in the spleen because it lacks hematogenous pigmentation and cells containing blood corpuscles are very rare. Let us note also that deposits of pigment are lacking also in other organs where they might be found as a result of excessive decomposition of blood.

Accordingly I think the most likely hypothesis is that the anemia is due to chronic poisoning whose source can lie only in the spleen, because the anemia disappears as soon as the spleen is eliminated. We might, in this connection, call attention to the fact that chronic sclerotic endophlebitis is occasionally found exclusively in the splenic vein while the other branches of the portal vein are healthy. Does this not seem to indicate that poisonous substances force their way forward through this vessel and that these substances may readily induce chronic inflammation of the vein, as other toxic substances are known to do?

Concerning the nature of the poison I do not know what to say.

Cirrhosis of the liver can not be looked upon as an accidental

complication, independent of the basic disease. The regularity of the stages of the disease, their typical serial order, and the absence of the usual causes of cirrhosis make such an assumption untenable. Nor can we trace it to the anemic condition because the anemia, itself, probably produces parenchymatous deteriorations but no hyperplasia of the connective tissue. It has also been assumed that it might be the result of poison generated in the intestine. Undoubtedly interstitial inflammation of the liver may develop from chronic dyspepsia, but can such an origin be assumed in the disease that I have described? I do not believe so because in most of the individuals attacked by this disease the gastric and intestinal functions remained completely normal except in the ascitic period, the appetite continued to be good, digestion was complete, and the discharges were regular. There were no signs of abnormal fermentation in stomach or intestine and therefore it would hardly be possible for toxic substances to form in these passages and then induce affection of the liver. It should be noted that cirrhosis of the liver induced by digestive disturbances is marked by noteworthy enlargement of the liver which rarely, and only after many years, passes over into an atrophic condition, whereas in the disease under discussion only a few months elapse between the beginning of the hepatic affection and complete atrophy of the liver.

Even back in 1894 I suspected that the affection of the liver must be a direct result of the affection of the spleen and now I am very much of the same opinion. At that time I assumed that toxic substances develop in the spleen and by invasion of the blood cause anemia. Then, because of their constant passage through the liver, they induce hyperplasia of the connective tissue in that organ with an action similar to that of alcohol absorbed by the intestine. It seems to me, likewise, that the chronic endophlebitis limited to the splenic vein permits us to conclude that there has been constant passage of poison through this vessel, since there is no other cause present to explain the origin of the condition. It should be added that in a case of splenomegalia with cirrhosis of the liver Prof. Colzi observed slight granulation of the liver when he performed splenectomy;

this was an unquestionable sign of beginning cirrhosis. In spite of this fact the patient recovered completely and at the time of writing, 21 months later, she was no longer showing any signs of anemia nor did she show evidence of any other affection of the liver. Therefore we know that extirpation of the spleen arrested the beginning cirrhosis; are we not justified in saying *sublata causa tollitur effectus*—by removing the cause, the effect is removed.

Concerning the actual causes of the disease I have no statement to make. All the bacteriological examinations have yielded only negative results, but in spite of this fact we cannot exclude the possibility of infectious origin; on the contrary, I am inclined to believe that, since there are no other causes evident, such an assumption would seem quite reasonable.

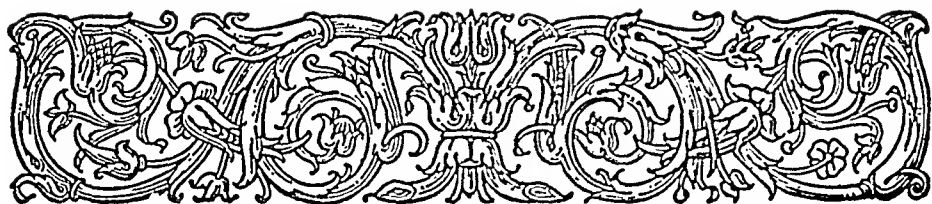
Since the original seat of the trouble lies in the spleen and since all medicinal treatment is without effect, splenectomy is urgently to be recommended. This is the only therapy even after hyperplasia of the connective tissue in the liver has set in, but operation should be performed before beginning of ascites. The operation statistics in the clinic in Florence are favorable because two of the three patients recovered completely and the third died of puerperal complications not connected with the operation.

*Florence, February 1898.*

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